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PSYCHOMOTOR EPILEPSY

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TYPES OF PAROXYSMAL SYNDROMES

WHEN a large, unselected group of epileptic patients is studied and the scope of the study is sufficiently broad to include clinical, electroencephalographic, anatomophysiologic and pharmacologic correlates, three major types of paroxysmal syndromes are distinguishable,[1] namely, convulsions, petit mal seizures and psychomotor seizures. The recognition of these three types of seizures does not exclude others, and doubtless subclassification is desirable; but the present distinctions are real and of practical importance.[2]

Convulsions.—These are common at all ages; they may be generalized or focal; they are associated with a sequence of fast spikes in the electroencephalogram [1a]; they are benefited by diphenylhydantoin sodium U. S. P. (dilantin®)[3] and methylphenylethyl hydantoin[4] (mesantoin®),

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1. (*a*) Gibbs, F. A.; Davis, H., and Lennox, W. G.: The Electroencephalogram in Epilepsy and in Conditions of Impaired Consciousness, Arch. Neurol. & Psychiat. **34**:1133 (Dec.) 1935. (*b*) Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Cerebral Dysrhythmias of Epilepsy: Measures for Their Control, ibid. **39**:293 (Feb.) 1938; (*c*) Influence of the Blood Sugar Level on the Wave and Spike Formation in Petit Mal Epilepsy, ibid. **41**:1111 (June) 1939. (*d*) Gibbs, F. A.: Electroencephalography in Epilepsy, J. Pediat. **15**:749, 1939. (*e*) Nims, L. F.; Gibbs, E. L.; Lennox, W. G.; Gibbs, F. A., and Williams, D.: Adjustment of Acid-Base Balance of Patients with Petit Mal Epilepsy to Overventilation, Arch. Neurol. & Psychiat. **43**:262 (Feb.) 1940. (*f*) Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Electroencephalographic Classification of Epileptic Patients and Control Subjects, ibid. **50**:111 (Aug.) 1943.

2. Gibbs, F. A.: New Drugs of Value in the Treatment of Epilepsy, Ann. Int. Med. **27**:548, 1947.

3. Merritt, H. H., and Putnam, T. J.: Sodium Diphenyl Hydantoinate in the Treatment of Convulsive Disorders, J. A. M. A. **111**:1068 (Sept. 17) 1938.

4. Kozol, H. L.: The Treatment of Epilepsy with Methylphenylethyl Hydantoin (Mesantoin), A. Research Nerv. & Ment. Dis., Proc. (1946) **26**:404, 1947.

two drugs which frequently make petit mal worse; they are also benefited by phenobarbital,[5] which rarely prevents petit mal and often increases psychomotor seizures.[5]

Petit Mal Seizures (pyknoleptic attacks).—Such attacks are common in children and rare in adults, tend to diminish with increasing age after the eighteenth year,[1f] are associated with approximately 3 per second wave and spike activity in the electroencephalogram.[1a] are often made worse by diphenylhydantoin sodium and are benefited by trimethadione (tridione®), a drug which commonly makes convulsions worse.[6]

Psychomotor Seizures (psychic equivalents).—These seizures, the subject of the present report, are rare in children and common in adults.[1f] With a reference electrode on the two ears, the electroencephalogram shows flat-topped waves, formed by a sequence of positive spikes.[1b] These seizures are rarely controlled by medication.[2] They can occur in the absence of convulsions or petit mal seizures. They are as distinctive as most other types of nervous dysfunction, and in the majority of cases a diagnosis can be made on clinical grounds alone. At present, however, psychomotor epilepsy usually goes unrecognized or is misdiagnosed because no provision is made for it in the diagnostic classification. Of necessity, therefore, the physician classifies a case of psychomotor epilepsy under whatever heading seems to him the approximately appropriate one—for example, hysteria, psychopathic personality or schizoid psychosis.

In the present report, the clinical syndrome of psychomotor epilepsy is described, and it is shown that this condition is associated with electroencephalographic evidence of seizure activity in one or both temporal areas.

MATERIAL AND METHOD

Three hundred patients with epilepsy whose electroencephalograms showed a psychomotor type of discharge were selected for special study. What is meant by the "psychomotor type of discharge" can be seen by reference to numerous illustrations [7] (fig. 1). In order to become familiar with all the varieties of psychomotor pattern, however, one should study one hundred or more classified original records. A verbal description of the pattern is necessarily so coarse that it is invalid for

5. Hauptmann, A.: Luminal bei Epilepsie, München. med. Wchnschr. **54**:1907, 1912.

6. Lennox, W. G.: Petit Mal Epilepsies: Their Treatment with Tridione, J. A. M. A. **129**:1069 (Dec. 15) 1945. Perlstein, M. A., and Andelman, M. B.: Tridione: Its Use in Convulsive and Related Disorders J. Pediat. **29**:20 1946. Lennox, W. G., and Davis, J. P.: Effects of Trimethyloxazolidine Dione (Tridione) and of Dimethylethyloxazolidine Dione on Seizures and on the Blood, A. Research Nerv. & Ment. Dis., Proc. (1946) **26**:423, 1947.

7. Gibbs, F. A., and Gibbs, E. L.: Atlas of Electroencephalography, Cambridge, Mass., Lew A. Cummings Co., 1941, p. 221.

diagnostic purposes, but a word picture of the pattern, recorded with the reference electrode on both ears, is conveyed by the following statement: The basic unit of the psychomotor discharge is a positive spike, which may be short in duration, and therefore definitely spikelike in appearance (when recorded at the standard speed of 3 cm. per second), or long in duration, for example, one-fourth second, so that it looks like a wide, blunt or saw-toothed wave. The terms "fast spike" and "slow spike" are used to describe these varieties. Usually, when the spikes occur between seizures, they are from five seconds to five minutes apart. However, when a seizure is impending, they tend to come closer together, and sometimes occur in bursts, with the spike repeating approximately four times a second to form flat-topped waves of that frequency. Such bursts are termed "larval psychomotor seizure discharges." After such a discharge, or mixed with it, there are often high voltage waves with a frequency of approximately 6 per second. If a record is obtained during a clini-

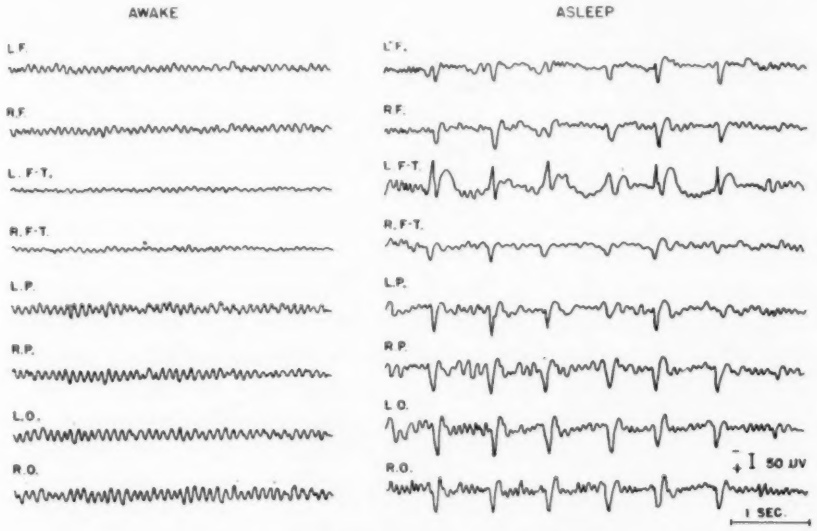

Fig. 1—Psychomotor types of discharge showing only during sleep.

cally evident psychomotor seizure, the pattern is that of a larval seizure except that it is more prolonged and the 6 per second waves become more prominent.

In the present study, 149 patients were studied only while awake. However, because of the evidence of increased seizure discharges during sleep,[8] 111 patients were studied during natural sleep and 40 during sleep induced with thiopental sodium U.S.P. ("pentothal").

Electroencephalograms were taken on either a six or an eight channel Grass electroencephalograph. In all cases the ears were used together as a reference electrode, and then each ear was used separately. The reference electrode was

8. (*a*) Gibbs, E. L., and Gibbs, F. A.: Diagnostic and Localizing Value of Electroencephalographic Studies in Sleep, A. Research Nerv. & Ment. Dis., Proc. (1946) **26**:366, 1947. (*b*) Fuster, B.; Gibbs, E. L., and Gibbs, F. A.: Anterior Temporal Localization of Negative Spike Discharges During Spontaneous or Induced Sleep Electroencephalogram in Psychomotor Epilepsy read at the Second South-American Neuro-Surgical Meeting at Chile April 25, 1947.

often moved to the nose, chin, nape of the neck or vertex. "Bipolar" leads in a row, in a triangle or in a circle were frequently employed, as was also a lead from high in the nasopharynx.

RESULTS

The group under investigation was selected on the basis of an electroencephalographic diagnosis of psychomotor epilepsy, and it was

TABLE 1.—*Incidence of Different Types of Clinical Seizures in 300 Patients with Psychomotor Seizure Discharge*

Type of Clinical Seizure	No. of Patients	Percentage of Total Series	
Grand mal and psychomotor	199	66.3	90
Psychomotor only	61	20.3	
Focal and psychomotor	10	3.4	
Grand mal only	27	9.0	10
Focal only	3	1.0	
Total	300	100.0	

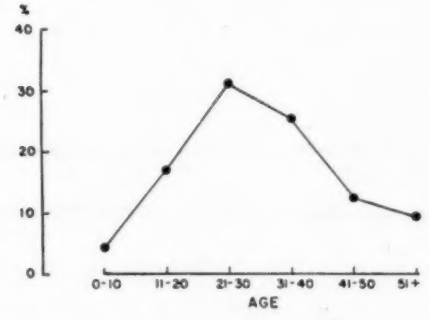

Fig. 2.—Age dstribution of 300 patients with electroencephalograms of psychomotor type in terms of percentages of the total group falling within a given age range.

of interest to determine the degree of association with clinical psychomotor seizures. Table 1 shows that there was a clear history of psychomotor seizures in 90 per cent of the cases; the association was higher with psychomotor seizures than with any other type of seizure.

The age distribution of the present series is in accord with the previous observation [1f] that psychomotor epilepsy is commoner in adults than in children (fig. 2).

Clinical Features of the Psychomotor Seizure.—The chief clinical manifestations of psychomotor seziures may be described as follows: The patient becomes confused and, as a rule, amnesic, but does not usually lose consciousness. His movements appear purposeful but are poorly coordinated, and his manner is frequently negativistic. In general, his behavior is that of a person acting out a bad dream. Often, during the

seizure there are manifestations of fear or rage with screaming or shouting. In most seizures the movements are simple, repetitive and more or less automatic; the chief behavioral elements are shown in the following tabulation.

Incoordination	Chewing	Rubbing
Negativism	Swallowing	Plucking
Staring	Spitting	Undressing
Pushing	Smacking the lips	Shouting
Groping	Laughing	Screaming
Searching	Crying	Confused talking

In some seizures the movements are more elaborate and clearly purposeful; speech may be unaffected except as regards content. Usually in the interseizure period severe personality disorders are present. These may be of such high degree that the patient is classified as psychotic. Irrespective of medication, hypersomnolence is common.

The Psychomotor Focus.—As previously stated, with the standard "monopolar" recording, i.e., with reference electrodes on the two ears, the outstanding feature of the psychomotor discharge is the positive spike. This usually appears in all leads except the temporal, in which flattening of activity or a negative spike is commonly observed. If only one temporal area is affected and the ear lead on that side is disconnected, so that the opposite ear is used as a reference, the generalized positive spikes disappear or are greatly decreased in amplitude, and the focus of negative spikes stands out clearly in the anterior temporal area. Thus, it appears that the anterior temporal area is involved in a disturbance the high voltage activity of which spreads to the ear on the affected side. When an active ear lead forms part of the reference electrode, the activity shows in all leads, unless canceled or reversed in phase by equal or greater activity from a scalp electrode. The localization and area of spread of the psychomotor type of focus are shown in figure 3 *A* and *B*.

The incidence of foci in the left and right temporal areas and of bilaterally independent foci is shown in figure 4. The psychomotor type of focus can be localized with "bipolar" leads, placed either in a row or in a triangle, though the task seems simpler to us when a common, or reference, electrode is used. If bipolar leads are used, one must be on guard against false localizations due to cancelation of seizure activity over the center of the focus and exaggeration of activity at its border. A precise localization requires that some electrodes be placed "off the brain," i.e., low on the head, over relatively inactive areas.

The spread of the psychomotor discharge is characteristic; it explains the positive spikes in all leads when recorded with a reference electrode formed by interconnecting the ear lobes. Not all spikes from the temporal lobe spread to give a psychomotor type of discharge. Nonspreading spikes of equal and higher voltage are commonly obtained from the mid-

temporal area. The spread seems to be peculiar to spikes from the anterior temporal area. The sharpest localization is obtainable when spike activity is submaximal, and not during a clinical seizure, for

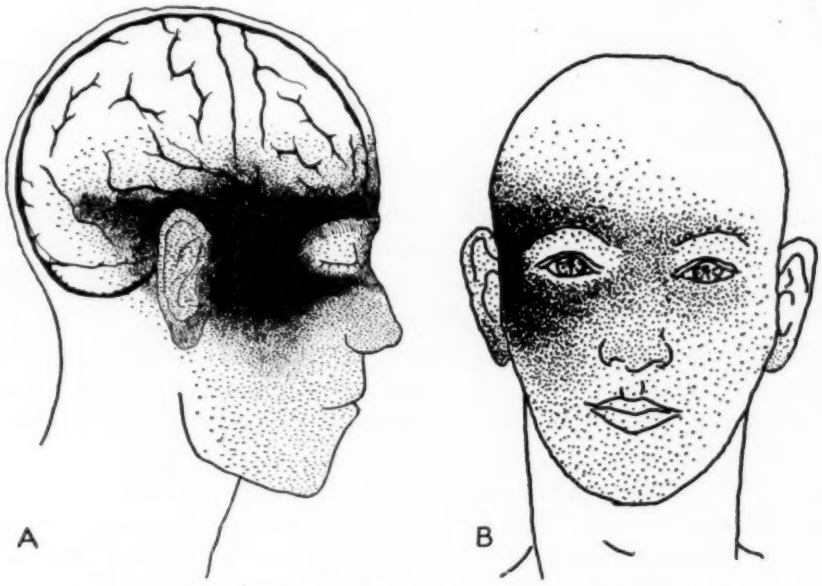

Fig. 3.—Location and area of spread of the psychomotor focus.

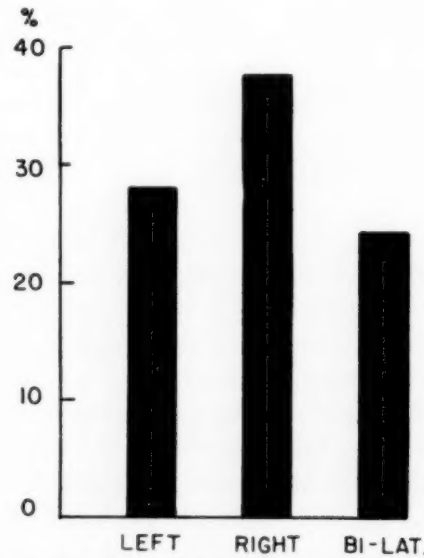

Fig. 4.—Incidence of foci in the left and right temporal areas and of bilaterally independent foci of psychomotor type (300 cases).

then the discharge becomes more or less generalized and is mixed with diffuse, high voltage, 6 per second activity. As previously reported, the focus shows best during natural [8a] or induced [8b] sleep, at which

time it may develop so great a voltage and rhythmicity that it looks like the electrocardiogram.

Associated Signs and Symptoms.—Because the electroencephalographic findings suggsted damage in the temporal region, a search was

TABLE 2.—*Incidence of Neurologic Signs Referable to Temporal Lobe or Adjacent Regions in 300 Patients with Psychomotor Seizure Discharge*

Localizing Signs	No. of Patients	Percentage of Total Series*
Focal seizures	13	4.3
Hemiplegia	11	3.7
Aphasia	2	0.7
Hearing defect	3	1.0
Hemianopsia	2	0.7

* Because some patients had several localizing signs, addition of the percentages in this table does not give the total percentage of patients with such signs (see table 3).

TABLE 3.—*Incidence of Different Types of Aura in 300 Patients with Psychomotor Seizure Discharge*

Type of Aura	No. of Patients	Percentage of Total Series
Gastric	60	20.0
Visual	12	4.0
Auditory	8	2.7
Olfactory	7	2.3
Gustatory	4	1.3
Déjà vu	4	1.3
Fear	4	1.3
Aphasia	2	0.7
Tingling	2	0.7
Pain	2	0.7

TABLE 4.—*History of Clinical Diagnosis of Psychiatric Disorder in 300 Patients with Psychomotor Seizure Discharge*

Indications of Psychiatric Disorder*	No. of Patients	Percentage of Total Seizures
Severe personality disturbances	125	42.0
Suicidal attempt	8	2.6
Undiagnosed psychosis	18	6.0
Schizophrenia	5	1.7
Manic-depressive psychosis	5	1.7
Shock therapy	5	1.7

* All the patients who had severe aberrations of behavior are grouped together under the heading, "Severe personality disturbances," but specific (not exclusive) symptoms or evidences of disorder are listed also. Since the same case is represented more than once, the percentages should not be added (see table 5).

TABLE 5.—*Comparative Incidence of Signs Referable to Temporal Lobe and Personality Disturbances in 300 Patients with Psychomotor Epilepsy*

Signs Referable to Temporal Lobe		Severe Personality Disturbances	
No.	%	No.	%
42	14	125	42

made for other evidence of such damage. That there was a low incidence of neurologic signs referable to the temporal lobe or neighboring regions is shown in table 2. The incidence of auras, some of

which might indicate a disorder of the temporal lobe, are shown in table 3. By way of contrast, the high incidence of psychiatric manifestations is shown in table 4. The contrast is summarized in table 5, where it will be seen that only 14 per cent of the patients had neurologic signs suggesting involvement of the temporal lobe, whereas 42 per cent had personality disturbances.

Discussion of the etiology of the psychomotor type of focus would be pure speculation at present. In a minority of cases a history of head injury in the temporal area was obtained, but in the majority no history suggestive of damage to the brain could be elicited. The incidence of a family history of seizures in near relatives was 4.5 per cent, which is as high as that in Lennox's series of cases of idiopathic epilepsy (table 6), suggesting that a constitutional factor may be important, and hence implying that one type of focus is inheritable.

The epileptic personality is rare in patients with pure petit mal or grand mal seizures but is common in patients with psychomotor epilepsy.

TABLE 6.—*Incidence of a History of Epilepsy in Near Relatives of Patients with Different Types of Epilepsy*

	History of Epilepsy in Near Relative, %
Patients with psychomotor type of focus	4.5
Patients with idiopathic epilepsy (Lennox)	3.2
Patients with symptomatic epilepsy (Lennox)	1.3

In view of the high association of personality disorders with psychomotor epilepsy, it seems reasonable to attribute much of what has been called the epileptic personality to disturbances in the anterior temporal area. Belinson [9] reported a higher incidence of psychomotor epilepsy (26 per cent) in institutionalized epileptic patients and pointed out that this type of seizure and its behavioral concomitants are poorly tolerated by the community.

SUMMARY AND CONCLUSIONS

Three hundred patients with epilepsy whose electroencephalogram showed a psychomotor type of discharge were studied; 90 per cent had a history of clinical psychomotor seizures. In all cases a spike focus could be demonstrated in the anterior temporal area on one or both sides. This focus was most readily demonstrable during natural or induced sleep.

Psychomotor epilepsy is a specific epileptic syndrome characterized by clinical psychomotor seizures and by an epileptic type of involvement

9. Belinson, L.: Electroencephalographic Characteristics of Institutionalized Epileptics, Am. J. Ment. Deficiency **52**:5 (July) 1947.

of the anterior portion of the temporal lobe, as evidenced by a focus of spike seizure activity in that area; it is usually associated with personality disorder.

The incidence of epilepsy in near relatives of patients with a psychomotor type of focus is almost ten times as high as in the general population and at least as great as the familial incidence of "idiopathic" epilepsy. This suggests that the tendency to a focus in the anterior temporal area can be inherited.

Patients with psychomotor epilepsy are rarely benefited by treatment with any or all of the antiepileptic substances at present available. The focus is located in an accessible "silent area." In severe cases surgical removal of the discharging region should be attempted.

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THE HUMAN ELECTROMYOGRAM IN RESPONSE TO NERVE STIMULATION AND THE CONDUCTION VELOCITY OF MOTOR AXONS

Studies on Normal and on Injured Peripheral Nerves

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ELECTROMYOGRAPHIC technics can be employed to obtain a quantitative measure of the functional impairment in man resulting from injury to peripheral nerve fibers or from other causes which prevent the passage of impulses along motor nerve fibers or across neuromuscular junctions. In the studies of nerve trauma to be described in this paper, the damaged nerve was activated by electrical stimuli delivered through the skin. The stimulating shocks were strong enough to activate all the excitable skeletomotor fibers in the nerve. The muscle action potential was recorded through small electrodes on the skin overlying appropriate muscles; this was the combined potential of many individual muscle fibers. The magnitude of this response was therefore determined, in part, by the number of muscle fibers which were functionally innervated and could, accordingly, be used to detect changes in this number, for example, during regeneration of an injured nerve. In addition, the conduction velocities of the motor nerve fibers were calculated from the latency of the muscle action potential. Since the velocity is known to be in direct proportion to the diameter of the axon, the size of growing axons could thus be determined at any stage of recovery.

The amplitude of the muscle action potential was similarly measured by Harvey and Masland [1] in studies on the abductor muscle of the fifth finger in cases of myasthenia gravis, and in a number of other muscles by Harvey and Kuffler [2] and Harvey, Kuffler and Tredway [3] in cases of peripheral neuritis and hysterical paralysis.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Pennsylvania.

1. Harvey, A. M., and Masland, R. L.: The Electromyogram in Myasthenia Gravis, Bull. Johns Hopkins Hosp. **69**:1-13, 191.

It is our purpose in the present paper to describe procedures for applying this method of electromyography to all the important muscle groups of the forearm, hand, leg and foot and to illustrate its use in measurements on normal subjects, on patients with peripheral nerve injuries and on patients with hysterical paralysis. This method, in which the motor nerve is stimulated electrically, is to be distinguished from that in which the electromyogram is recorded during maximal voluntary effort. The latter procedure relies on the cooperation of the patient and is technically more difficult to make quantitative. In addition, complications may result from the notable difficulty in voluntarily confining activity to a particular muscle group during maximal effort.

METHODS

Position of Patient.—The support shown in the three parts of figure 1 was convenient for examination of nerves in the forearm. With the patient seated, his hand was strapped to a padded block, his arm being supported in different ways for testing the various nerves.

When the ulnar nerve was tested, the arm rested horizontally in a U-shaped block, with the elbow bent at right angles (fig. 1, upper part). This position was important, since it made the nerve much easier to stimulate than when the elbow was straightened. The hand was approximately pronated, being tipped slightly one way or the other to facilitate the placing of electrodes over the abductor digiti quinti or the first dorsal interosseous muscle. For examination of the latter muscle, the thumb was held in abduction by the adjustable block, shown in the lower part of figure 1.

For tests of the radial nerve the arm was supported in a similar position (fig. 1, center portion), except that the elbow rested on a flat, padded block, since the U block used in tests of the ulnar nerve displaced the muscles of the arm so that the radial nerve was difficult to stimulate.

For stimulation of the median nerve the hand was supinated, with the arm directed forward from the shoulder (fig. 1, lower portion). When records were being made from the thenar muscles, the thumb was held abducted by the adjustable block.

For examinations of nerves of the leg the patient lay outstretched on a bed, prone for tests of the tibial nerve and on his back for tests of the peroneal nerve.

Stimulation.—The stimuli were brief condenser discharges, usually at the rate of about 1 per second, controlled by a gas tetrode and delivered to the electrodes through an isolating transformer in order to minimize the stimulus artefact. The intensity was adjusted by means of a potentiometer in the primary circuit.

The stimulating electrodes consisted of two brass cups about ¾ inch (1.9 cm.) in diameter and ⅜ inch (0.95 cm.) deep. These were filled with absorbent cotton, held in place by several layers of gauze tied over the rim of the cup. The electrodes

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2. Harvey, A. M., and Kuffler, S. W.: Motor Nerve Function with Lesions of the Peripheral Nerves: A Quantitative Study, Arch. Neurol. & Psychiat. **52**:317-322 (Oct.) 1944.

3. Harvey, A. M.; Kuffler, S. W., and Tredway, J. B.: Peripheral Neuritis: Clinical and Physiological Observations on a Series of Twenty Cases of Unknown Etiology, Bull. Johns Hopkins Hosp. **77**:83-103, 1945.

were soaked in saline solution before application to the skin in order to insure good electrical contact over the entire area of each electrode and thus prevent painful concentration of the current. The cups were mounted 1 to 2 inches (2.5 to 5 cm.) apart on a "bakelite" strip and handle. This could be held in place by hand, by a rubber band passing around the patient's extremity (fig. 1) or by clamps attached to the support used in examinations of the forearm.

It is of the utmost importance to avoid inadvertent stimulation of nerves in the vicinity of the one under test, for reasons which will be given later. The various nerves, therefore, were commonly stimulated at the following points, which are

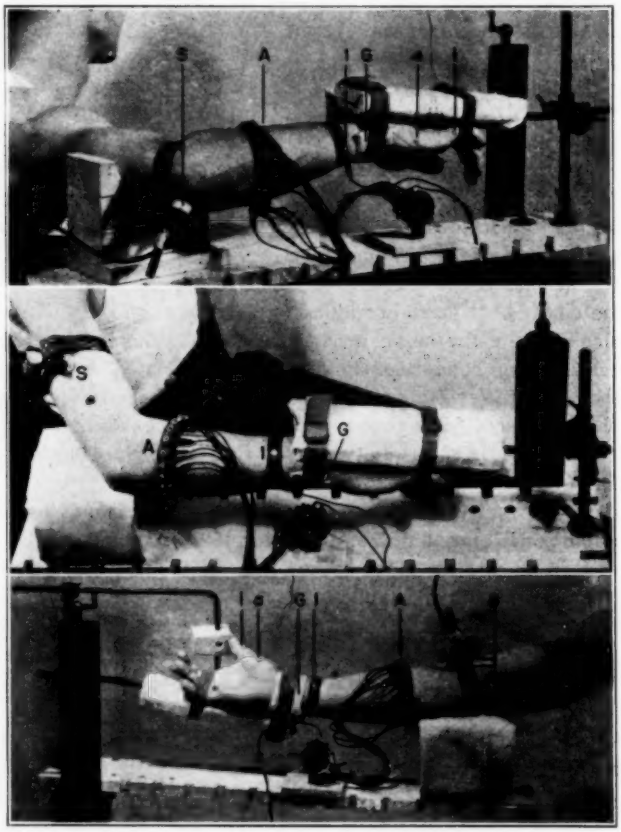

Fig. 1.—Support and arrangement of electrodes for examinations of the ulnar nerve (upper picture), the radial nerve (center picture) and the median nerve (lower picture). *A* and *I* are active and indifferent electrodes for recording from muscles of the forearm; *a* and *i* are active and indifferent electrodes for recording from muscles of the hand; *G* is the ground electrode, and *S* is the pair of stimulating electrodes.

conveniently accessible and as well isolated as possible from neighboring nerves: ulnar nerve, at the elbow or wrist; median nerve, on the flexor surface of the forearm just distal to the elbow, on the medial surface of the arm just above the elbow, or at the wrist; radial nerve, on the lateral surface of the arm about halfway between the axilla and the elbow (it was difficult to excite the deep branch of the radial nerve at positions closer to the elbow than this); tibial nerve, in the

lower limits of the popliteal space (it was sometimes difficult to avoid spread to the peroneal nerve) or at the ankle; peroneal nerve, on the lateral surface of the leg just below the knee, or at the ankle. In some cases it was, of course, necessary to modify these procedures, owing to a thick scar or a transposed nerve.

By trial on each patient, the position for the stimulating electrodes was found which permitted excitation of the desired nerve with the smallest possible current. This reduced the likelihood of spread of stimulus to other nerves and usually permitted generously supramaximal stimulation of all motor fibers to the muscles under examination with little, or no, discomfort to the patient.

Since the accuracy of the method which we have employed depends on stimulation of all the motor fibers to the muscles being tested, the following checks were made to be certain that the stimuli were strong enough to accomplish this. The strength was first varied while the examiner watched on the cathode ray tube the responses to single shocks repeated about once a second. After the minimum intensity which just sufficed to elicit a maximal response was determined, further tests were made with a shock at least 50 per cent stronger than the just maximal strength. In a few subjects with injured nerves the amplitude of response increased with strength of stimulus up to the strongest shocks that could be tolerated, so that no reliable quantitative measurements could be made. This difficulty arose most often in cases in which the damage was in the proximal part of an extremity, necessitating stimulation of the nerve in its regenerating portion; here, the axons are known to be of lowered irritability.[4]

Methods of Recording.—The muscle action potentials were amplified by a three stage, condenser-coupled differential amplifier and either observed directly on a 3 inch portable cathode ray oscilloscope or photographed from a 5 inch blue screen oscilloscope. The sensitivity of the amplifier was determined by daily calibration.

For measurement of the action potentials of the small muscles in the hand or foot, the two leads to the input of the amplifier consisted of light flexible wire (no. 36 B. and S. gage) soldered to ¼ inch (6 mm.) squares of silver or copper foil. These squares were satisfactorily held in place on the skin with small dabs of electrocardiographic electrode paste (fig. 1) and could easily be moved about, thus making it possible to record from a number of positions in rapid succession. At the beginning of an examination, one of the electrodes (the active electrode) was placed over the belly of the muscle being tested and the other (the indifferent electrode) over the tendon. After the stimulus was adjusted to a supramaximal value, as previously described, the active electrode was tried in a number of locations while the responses on the cathode ray oscillograph were observed. When the position which yielded the largest action potential was found, the response was photographed for permanent record, or its amplitude was measured directly on the cathode ray screen.

For similar selection of the optimum position of the active electrode over the long muscles of the forearm or the leg, a multiple electrode assembly was constructed of eleven small brass cups mounted at ½ inch (1.3 cm.) intervals on a rubber band, which could be fastened around the extremity (fig. 1). Each cup was filled with a cotton plug, which was moistened with saline solution before being brought into contact with the skin. The wires from these eleven electrodes led to a selector switch. Measurements were usually made with this electrode assembly at a number of distances below the elbow or knee, in order to determine the degree of function at several distances from the site of nerve injury. At each position

4. Erlanger, J., and Schoepfle, G. M.: A Study of Nerve Degeneration and Regeneration, Am. J. Physiol. **147**:550-581, 1946.

the only measurement of interest was usually that obtained through the electrode yielding the largest response, except that in tests of the radial nerve records were routinely taken over both the brachioradialis muscle and the superficial extensor muscle. The indifferent electrode was a single similar brass cup placed over the tendons of the muscles being examined.

In order to minimize extraneous electrical interference, the patient was connected to ground through a sheet of copper covered with gauze soaked in saline solution and usually strapped around the wrist or ankle of the extremity being tested. For examinations of the forearm, the strap holding this ground electrode passed around the padded block (fig. 1), thus forming an integral part of the support for the hand. Most examinations were conducted in a room which was in part electrically shielded.

Limitations and Precautions Required Because of Spread of the Action Potential.—The action potential of a particular muscle could be detected through electrodes placed not only on the skin directly overlying it, but also on the skin over

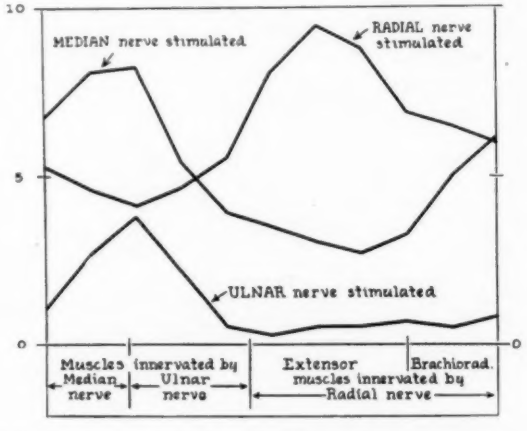

Fig. 2.—Spread of muscle action potentials in the forearm, 4 inches (10 cm.) below the olecranon, in a normal subject. The amplitude of the action potential in response to supramaximal stimulation of each of the three nerves is plotted for eleven positions of the active recording electrode equally spaced around the circumference of the forearm. The approximate relation of these electrode positions to the various muscle groups is indicated at the bottom of the graph. Amplitude (ordinate) is expressed in millivolts.

nearby muscles. This fact requires careful consideration in any percutaneous electromyographic recording. One consequence was the impossibility of accurately measuring the action potential of one muscle when neighboring ones were simultaneously in action, for the recorded potential was then an unresolvable summation of their several contributions. The best that could be done was to restrict carefully the stimulation to a particular nerve and then measure the potential resulting from the collective action of all the muscles in the group innervated by it. This was usually satisfactory in the examination of patients with peripheral nerve injuries, since interest was centered on recovery of the function of an entire nerve trunk, rather than of the nerve fibers supplying any particular muscle.

The spread of muscle action potentials circumferentially around a limb is illustrated in figure 2, in which the responses were recorded through eleven electrodes spaced approximately equally around the forearm, 4 inches (10 cm.) below the

olecranon. At the bottom are indicated the approximate positions of the muscle groups supplied by the median, ulnar and radial nerves. Each curve represents the amplitude of the action potential at the various electrodes when the indicated nerve was stimulated. The most remarkable spread was shown by the action potential of the muscles supplied by the radial nerve, which at its minimum was still nearly half as great as the value obtained directly over the extensor muscles. Obviously, inadvertent spread of stimulus to the radial nerve would invalidate any measurement attempted for the median or the ulnar nerve. The spatial overlap of the responses to stimulation of the ulnar or median nerve is another important point, for separate stimulation of these two nerves sometimes became difficult after the ulnar nerve had been transposed to a position near the median nerve in suture operations. Under this condition, it was occasionally impossible to make a satisfactory test of either of these two nerves.

Because of the errors which can thus result from spread of stimulus, careful checks against activation of nerves other than the one being tested were always made by watching the motion produced and by palpating appropriate muscles and tendons.

THE NORMAL ELECTROMYOGRAM AND THE NORMAL CONDUCTION VELOCITY OF MOTOR NERVE FIBERS

Form of the Muscle Action Potential.—In figure 3 are examples of the normal action potentials of the muscles and muscle groups employed in our investigations. In addition to the muscles for which records are illustrated, a few trials indicated that a similar technic could probably be employed with certain facial muscles. The deflections in most records started with a brief artefact (labeled *S*) caused by the stimulus, followed by an interval (the latent period) before the muscle action potential began. The action potential commenced with an upward deflection, caused by a negative change in potential under the active recording electrode, which was over the belly of the muscle. This was followed by a downward deflection, which was presumably due to a number of causes, including a negative variation near the indifferent electrode (over the tendon of the muscle), activity in muscle fibers not directly under either electrode and possibly also a positive variation at the active electrode. This downward deflection was not of particular interest in the present investigation, since we were concerned only with those events in the vicinity of the active electrode which were measured by the initial, upward component of the action potential record. The number of muscle fibers taking part in this activity was indicated by the amplitude of the upward deflection, measured in millivolts from the level of the base line before stimulation. Certain qualifications of this statement will be discussed later.

The action potentials of the small muscles of the hand or foot were usually simple in form, the upward deflection having a smooth contour with only one peak (fig. 3). In contrast, the action potentials of the long muscles of the arm or leg were usually more complicated,

exhibiting several crests (fig. 3). Even for a particular muscle group, the relative heights of the various crests varied from one subject to another, as well as with the location of the active recording electrode. As this electrode was moved in small steps around the circumference of an extremity, for example, a particular peak would grow in prominence and then recede as another grew, with further displacement of the electrode (fig. 4). Evidently, the several peaks were contributed by different muscles (or, possibly, by different parts of the same muscle),

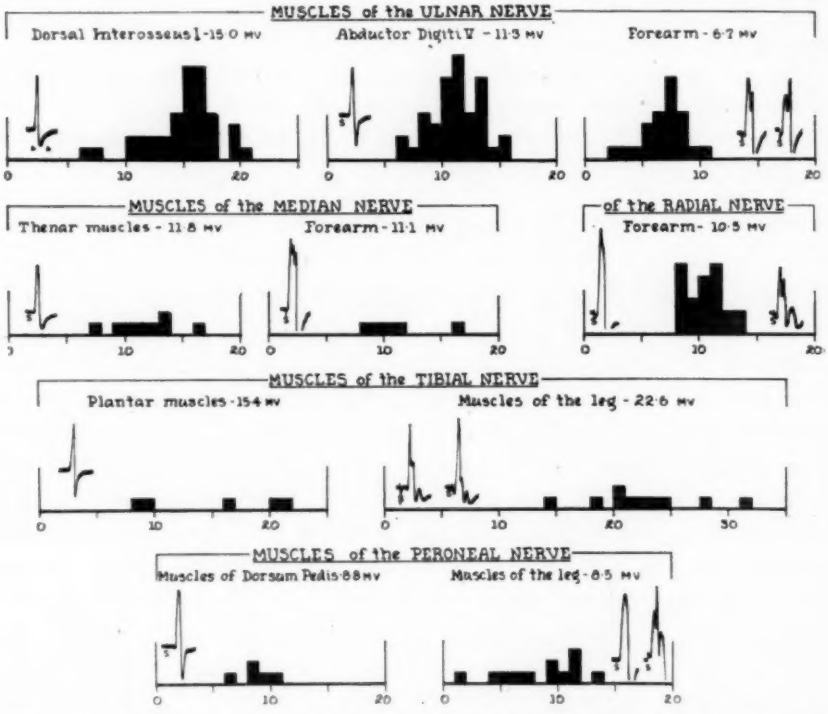

Fig. 3.—Normal action potentials recorded with electrodes over various muscles, in response to supramaximal stimulation of appropriate nerves. The histograms indicate the distribution of amplitudes in a number of observations, the abscissas being marked in millivolts. The average amplitude is given after the name of each muscle.

The records of action potentials illustrate the form of response at the electrode position yielding the maximal amplitude for the short muscles in the hand and foot, and at the following positions for the muscles of the forearms and leg: Forearm: muscles of the ulnar nerve, 6 and 4 inches (15 and 10 cm.) below the olecranon; muscles of the median nerve, 4½ inches (11.5 cm.) below the olecranon; muscles of the radial nerve, 4 inches below the olecranon, the first record being over the extensor muscles and the second over the brachioradialis muscle of the same subject. Leg: muscles of the tibial nerve, 8 and 4 inches (20 and 10 cm.) below the tuberosity of the tibia; muscles of the peroneal nerve, 6 and 4 inches (15 and 10 cm.) below the tuberosity of the tibia.

The time scale, which is the same for all records, is indicated by marks 1/60 second apart at the bottom of the upper left record. *S* indicates the stimulus artefact in records in which it could be identified. Records in this illustration have been retouched where the cathode ray trace was too faint for satisfactory reproduction.

the various latencies of the peaks being due, presumably, to differences in the conduction velocity of the nerve fibers concerned. The identification of the particular muscle associated with each peak has, however, proved unnecessary and too difficult to be worth undertaking as part of the present investigation.

Latency of Response and Conduction Velocity of Motor Nerve Fibers.—The interval (latent period) between the instant of stimulation

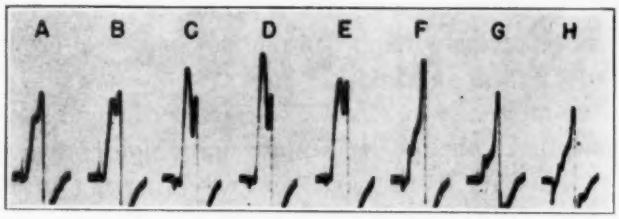

Fig. 4.—Change in the action potential of the muscles of the forearm of the ulnar nerve when the active recording electrode is moved in steps around the forearm 6 inches (15 cm.) below the olecranon. In record *E* the action potential has two components, which are of nearly equal height. The first component (latency of peak, 6.0 milliseconds) has its maximum at *D* and declines progressively as the electrode is moved away in either direction; the second component (latency of peak, 9.5 milliseconds) has its maximum at *F*.

Fig. 5.—*A*, difference in latency of response when a nerve is stimulated at two different distances from a muscle. Records were taken from the plantar muscles of the foot. In the upper record the tibial nerve was stimulated at the ankle; in the lower record, just below the knee. *S* indicates the stimulus artefact. The time interval is 1/60 second.

B, action potentials of muscles supplied by regenerating and by normal nerves. Records were taken at the same amplification from the left and the right abductor digiti quinti muscle in response to stimulation of the ulnar nerve at the elbow. The left ulnar nerve (upper record) had been sutured ten months previously, about 3 inches (7.6 cm.) above the muscle. The stimulus artefact is indicated by *S* in the lower record and by a brief downward deflection at the same position in the upper record. The time interval is 1/60 second.

and the start of the action potential was in large part due to the time required for the conduction of nerve impulses to the muscle from the point of stimulation. This could readily be shown by stimulating a

nerve at two different points along its course while recording the action potential of an appropriate muscle in the hand or foot. It was possible, for example, to stimulate the ulnar or median nerve at the elbow and wrist, or the tibial or peroneal nerve near the knee and ankle. It was then found that the latency of response was much shorter when the stimulating electrodes were nearer the muscle (fig. 5*A*). The change in latency when divided by the distance between the two points of stimulation yielded an accurate measure of the conduction velocity of the most rapidly conducting nerve fibers. This determination was done for the nerves supplying a number of muscles in several normal subjects, and the results appear in table 1.

The values ranged from 46 to 67 meters per second for the various nerves investigated. These velocities are much slower than those which have been reported for motor nerve fibers to other muscles of the limb.

TABLE 1.—*Conduction Velocity of Several Human Nerves*

		Conduction Velocity in Nerve (Meters/Sec.)				Residual Latency (Milliseconds)			
				Average Several Subjects				Average Several Subjects	
Nerve	Muscle	H*	L.*			H*	L*		
Ulnar	Abductor digiti quinti.....	62	65	67	..	2.2	1.6	2.8	...
		..	..	65	..	...	...	1.6	...
		..	..	59	64	...	...	2.6	2.2
Ulnar	Dorsal interosseous I.....	60	62	..	61	1.7	2.3	...	2.0
Median	Thenar group	60	66	..	63	2.4	2.6	...	2.5
Peroneal	Extensor digitorum brevis..	52	58	56	55	2.8	3.5	3.2	3.1
Tibial	Flexor digitorum brevis.....	47	52	46	48	2.9	1.4	3.8	2.7

* H and L represent two different subjects.

For example, the fastest peripheral nerve fibers in the cat conduct at about 116 meters per second.[5] These fastest fibers are also the largest,[6] and some of them have been shown by histologic studies to arise from ventral roots and pass into nerve branches to the leg muscles[7]; thus, they may be assumed to have motor functions. Moreover, Piper,[8] with technics similar to ours, found a conduction velocity of 123 meters per second in human motor fibers to the ulnar nerve supplying muscles of

5. Gasser, H. S.: The Classification of Nerve Fibers, Ohio J. Sc. **41**:145-159, 1941. Lloyd, D. P. C.: Conduction and Synaptic Transmission of Reflex Response to Stretch in Spinal Cats, J. Neurophysiol. **6**:317-326, 1943.

6. Gasser, H. S., and Grundfest, H.: Axon Diameters in Relation to the Spike Dimensions and the Conduction Velocity in Mammalian A Fibers, Am. J. Physiol. **127**:393-414, 1939.

7. Eccles, J. C., and Sherrington, C. S.: Numbers and Contraction Values of Individual Motor Units Examined in Some Muscles of the Limb, Proc. Roy. Soc. London, s.B **106**:326-357, 1930.

8. Piper, H.: Elektrophysiologie menschlicher Muskeln, Berlin, Julius Springer, 1912.

the forearm. We found a closely similar value in the 2 instances in which we measured velocity in fibers to these muscles. The slower velocities in table 1 were all measured in nerve fibers supplying muscles in the hand or foot. These most distal muscles are supplied by motor nerve fibers which conduct only about one-half as fast as some of the fibers to more proximal muscles.

Residual Latency.—The time required for nerve impulses to travel from the stimulating electrodes to the muscle may be calculated approximately by assuming that they are conducted all the way at the velocities determined in the preceding section. It was found, however, that the conduction times thus computed were somewhat less than the observed latency of the muscle action potential. In other words, there was a small residual latency in excess of the calculated conduction time. The values for this residual latency are given in the final columns of table 1. The latency was presumably contributed by (1) a slower velocity of conduction in the finer terminal portions of the nerve fibers than that measured in the nerve trunk, and (2) a delay at the neuromuscular junction.[9]

Amplitude of the Muscle Action Potential.—The average amplitudes of the normal action potentials are presented in figure 3, in which the individual observations are summarized graphically. The histograms were constructed from the largest potential that could be found by trying the active electrode in a number of positions on the skin over the appropriate muscle or muscle group. The relatively wide range of values found for a particular muscle was due in part to differences between subjects and in part to unexplained variability in the measurements. The unexplained variability was shown by 33 duplicate determinations on muscles in uninjured extremities, the successive observations being made at intervals of not less than two weeks. The average difference between duplicate determinations was 23 per cent, the greatest difference being 67 per cent. Both these variations and the differences between subjects were controlled so far as possible in our observations by comparing the values for the injured and those for the normal extremity in each patient.

THE ELECTROMYOGRAM AND THE CONDUCTION VELOCITY OF MOTOR NERVE FIBERS AFTER NERVE INJURY

General Description.—The notable changes in the electromyogram after nerve injury were (*a*) a reduction in amplitude (or absence) of the action potential and (*b*) an increase in the latent period (fig. 5 *B*).

9. Lorente de Nó, R.: The Synaptic Delay of the Motoneurones, Am. J. Physiol. **111**:272-282, 1935. Eccles, J. C., and O'Conner, W. J.: Responses Which Nerve Impulses Evoke in Mammalian Striated Muscles, J. Physiol. **97**:44-102, 1939.

The time course of recovery after various types of nerve lesions will be discussed later in this paper. It is our purpose in the present section to illustrate the types of abnormality encountered and to consider their proper interpretation.

The progressive return toward the normal action potential is illustrated in figure 6 *I* by records from patients in three stages of recovery following nerve suture. Record *A* shows the type of activity observed when a response first became detectable as the nerve regenerated. It consisted of small potential fluctuations, which started after a latency many times that of the normal response, and was dispersed over a period of 60 milliseconds.

At a later stage of recovery (fig. 6 *I, B*) a synchronized action potential began to appear; and the latency was shorter, although still considerably greater than normal. The action potential was still small and was typically irregular in contour, even for those muscles whose action poten-

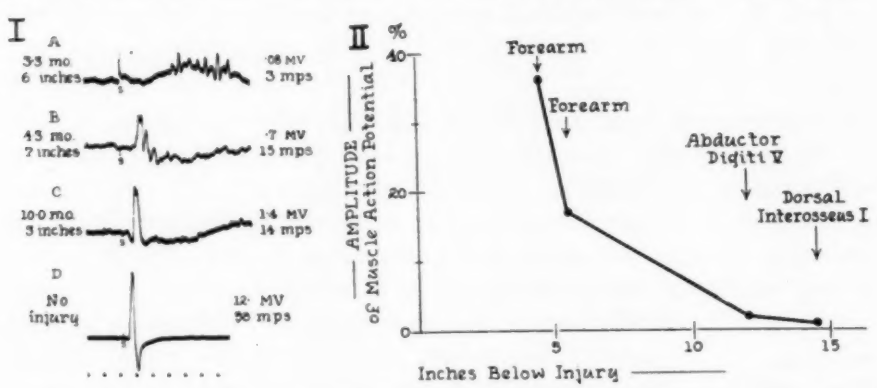

Fig. 6.—*I*, examples of muscle action potentials at various times after suture (*A. B. C*), as compared with the normal, in *D*. Records from the abductor digiti quinti muscle of various subjects in response to stimulation of the ulnar nerve at the elbow. To the left of each record is given the time since suture and the distance from the suture to the muscle. To the right are the amplitudes, expressed in millivolts, and the approximate conduction velocities of the regenerating portion of the nerve, calculated from total latency, as described in the text. *S* indicates the stimulus artefact. The time interval at the bottom is 1/60 second.

II, functional gradient in a patient recovering from an injury to the ulnar nerve at the elbow after neurolysis. The amplitudes of the action potentials of various muscles in response to supramaximal stimulation of the ulnar nerve are plotted against distance from the injury to the active recording electrode. The amplitudes are expressed as a percentage of amplitudes found at similar positions in the normal extremity of the same patient.

tials were usually simple in form. This irregularity appeared to result from the relatively small number of units in action, which were still too few for their individual potentials to summate into a smoothed curve. Indeed, it was occasionally noticed that a particular notch or crest would come and go in an all or nothing manner as the intensity of stimulus was slowly raised and lowered. This observation was best explained by

assuming that this particular component of the action potential was contributed by a group of muscle fibers all innervated by the same nerve fiber.

Later, as function was restored to a still larger number of muscle fibers, there was a further increase in amplitude of the action potential, and the contour became smoother (fig. 6*I*, *C*). These progressive changes toward normal continued in certain cases for many months, as will be further discussed in a later section.

Increase in Latency and Reduction in Conduction Velocity.—The latency of the action potential was always greatly increased in the early stages of recovery after nerve suture, and sometimes after spontaneous recovery. A large part of this increase was due to a reduced conduction velocity in the motor nerve fibers. The reduction in velocity has been shown in a few patients by determining the difference in latency between responses to stimulation at two different points on the regenerating portion of the nerve (table 2). The highest velocity thus found on three regenerating nerves ten or more months after suture was 60 per cent of normal. Slowed conduction following suture was also observed in the cat by Berry, Grundfest and Hinsey,[10] who found velocities less than 5 per cent of normal in the very earliest stages of recovery.

TABLE 2.—*Reduction in Velocity of Conduction in Regenerating Nerves*

Case No.	Nerve	Time	Percentage of Normal Velocity	Residual Latency, Milliseconds
1	Ulnar	10 mo. since suture	48	5.8
2	Ulnar	34 mo. since suture	48	3.4
3	Median	42 mo. since suture	60	3.4
4*	Ulnar	11 mo. since injury	55	3.0

* The nerve in case 4 recovered without operation.

We have found the velocity to be slowed not only after suture but also, in one nerve, during recovery without operation (table 2, case 4). It is certain, however, that many other nerves recovering without operation conducted at normal velocity, for in some such nerves the latency of response was found to be normal.

It has been shown in animal experiments that velocity varies in direct proportion to axon diameter during regeneration after suture,[10] as well as in normal adult nerves [6] and during the progressive increase in early growth.[11] Therefore our measurements of velocity demonstrate

10. Berry, C. M.; Grundfest, H., and Hinsey, J. C.: The Electrical Activity of Regenerating Nerves in the Cat, J. Neurophysiol. **7**:103-116, 1944.

11. Hursh, J. B.: Conduction Velocity and Diameter of Nerve Fibers, Am. J. Physiol. **127**:131-139, 1939.

that human axons, like those of animals,[12] remain of subnormal diameter for at least many months after suture. For example, the data in table 2 show that after the longest period of recovery in which our investigation was made (forty-two months, in case 3) the largest axons still had only 60 per cent of the velocity, and therefore, presumably, only about 60 per cent of the diameter, of the largest axons found in uninjured nerves. In the earlier phases of recovery, such as that shown in figure 6 *I, A*, in which the latency of response was increased manyfold, it is probable that velocity and diameter were much smaller still, although we have not accurately measured the velocity in any of these earlier stages.

Residual Latency.—The residual latencies, after allowance for conduction time at uniform velocity, are given in the final column of table 2. They were all greater than those found for the same muscles under normal conditions. Unfortunately, it was not possible to tell how much of this difference was due to an increased delay at the neuromuscular junction and how much to an unusual slowing of conduction in the terminal portions of the nerve fibers.

Temporal Dispersion.—Accompanying the increased latency of the start of the action potential, there was an increase in the duration of the potential (figs. 5 *B* and 6 *I*), indicating temporal dispersion of the responses of the various muscle fibers. The latter phenomenon, like the change in latency, is well explained by the slowed conduction of the nerve impulses. Even under normal conditions all the motor nerve fibers do not conduct at exactly the same rate, so that the nerve impulses, initiated simultaneously, do not all reach the muscle at the same instant. Therefore, a halving of conduction velocity in all fibers, for example, would result in a doubling of the conduction time in each, with a consequent doubling in the temporal dispersion with which the nerve impulses reach the muscle.

The increased temporal dispersion, presumably, does not significantly reduce the strength of voluntary muscular contraction, since this depends on summation of tension in motor units which usually act independently and quite asynchronously. The abnormal dispersion can, however, greatly reduce the amplitude of the electromyogram obtained by the method employed here, with technical consequences to be discussed in the next section.

Reduction in Amplitude.—Two factors must be assumed to contribute to the reduction in amplitude of the muscle action potential following nerve injury. One is an actual reduction in the number of innervated muscle fibers; the other is the increased temporal dispersion of the

12. (*a*) Berry and others.[10] (*b*) Gutmann, E.; Guttmann, L.; Medawar, P. B., and Young, J. Z.: The Rate of Regeneration of Nerve, J. Exper. Biol. **19**:14-44, 1942. (*c*) Young, J. Z.: The Functional Repair of Nervous Tissue, Physiol. Rev. **22**:318-374, 1942.

nerve impulses which excite them. The reduced innervation is of practical importance, for it limits the usefulness of the muscle. The dispersion is of less functional significance but must be considered in interpretation of the changes in amplitude. Thus, while a nerve is regenerating, and the conduction velocities of its constituent fibers are reduced, the consequent dispersion of the impulses as they reach the muscle results in a less synchronized activation, and therefore less summation of the action potentials of the individual muscle fibers. Hence, the recorded potential is reduced out of proportion to the degree of muscular denervation. With a further return toward normal, the temporal dispersion and its effects become less, so that the amplitude as compared with the normal becomes progressively a more accurate index of the percentage of muscle fibers reinnervated. Thus, in general, a simple proportionality between the amplitude of the action potential and other measures of function cannot be expected, the measurement of amplitude tending to underevaluation of function, particularly in the early stages of regeneration.

After recognizing the limitations described in the preceding paragraph, we considered using as a measure of activity the area under the initial deflection of the electromyogram, instead of simply the amplitude. Difficulty arose, however, from the diphasic character of the response, for it seemed likely that activity contributing the second (downward) phase began before completion of the activity contributing the initial (upward) deflection. Hence, the area under the upward deflection had no simple interpretation, being determined in part by relative timing of activity in different regions of the muscle. For this reason, we have studied the amplitude rather than the area of the muscle action potential, since the former was the easier to measure.

The amplitude of the action potential is a useful index, for it increases progressively during recovery, owing to the gradual return toward normal of both factors which contribute to its reduction. It can, accordingly, be used for comparative purposes, for example, to determine whether function has improved during the interval between two examinations, or whether there is at a particular time any difference in degree of muscular reinnervation at different distances from the lesion (table 3). In addition, in a later section, we shall present data on the rate at which the amplitude can be expected to recover after various kinds of injury. These data, by comparison, provide an empiric indication of whether improvement is lagging in any particular patient.

Functional Gradients.—It is well known that as function is restored after an injury which has caused degeneration of peripheral nerve fibers, the growing axons reinnervate the more proximal muscles first, the more distal muscles recovering only after an additional delay. Moreover, within the larger muscles, such as those of the forearm or leg, nerve

axons reach many muscle fibers in the upper portion of the muscle before there is any detectable innervation in the distal end of the same muscle. In other words, there exists in the earlier stages of recovery a "functional gradient" along the distribution of the nerve, the degree of function being greatest in the muscles or parts of muscles closest to the injury.

These functional gradients can be strikingly demonstrated by stimulating an injured ulnar nerve at the elbow, for example, and recording the action potential of a number of muscles innervated by it. A typical result is shown in figure 6*II* for a patient who had regained function after neurolysis. Similar functional gradients were measured in cases of recovery after nerve suture, as well as in cases of spontaneous recovery without operation (table 3). These cases will be discussed later, when the rates of recovery after various types of injury and repair are considered.

TABLE 3.—*Progressive Recovery of Amplitude of Muscle Action Potential After Nerve Injury*

Subject		Months After Suture	Percentage of Amplitude*	
			Abductor Digiti Quinti	Dorsal Interosseous I
A	Ulnar nerve sutured at wrist eight months after injury	1.5	0	0
		3.9	1.5	0.4
		5.4	8.0	2.0
B	Ulnar nerve sutured in midforearm four months after injury	4.3	8	2
		10.3	25	18
		Months After Injury		
C	Ulnar nerve recovering without nerve surgery after injury 3 inches above wrist	7.0	30	2
		8.3	39	4
		10.8	55	21

* Amplitude is expressed as a percentage of that for the corresponding muscle in the normal extremity of the same subject.

A quantitative measure of the functional gradient, which can thus be obtained by electromyographic technics, may furnish a valuable prognostic sign. When, for example, the degree of innervation after nerve injury is found to be much larger close to the lesion than more distally, it is probable that many axons have grown past the point of injury but have not had time to reach the more distal muscles in great number. Therefore good progress may be expected.

Correlation of Amplitude of Action Potential with Muscle Strength.—In many of our cases the amplitude of the muscle action potential was compared with the estimated strength of a maximal voluntary contraction. In figure 7 are shown the relative amplitudes of action potentials for muscles in each of the strength categories defined in the legend. It is obvious that the larger action potentials were found only in the stronger muscles and that at intermediate degrees of recovery there was a correlation between the average of the action potentials and the

estimated strength. The results of individual tests, however, revealed many exceptions to any simple relationship; this requires special comment.

In the first place, no action potential was detected in many cases in which strength was estimated as a "trace" or "poor." This indicates that, owing to limits in sensitivity of electrical recording, the action potential picked up from the surface of the skin was not a reliable index of the earliest stages of recovery. Presumably, activity could be detected under these conditions by means of needle electrodes thrust into the muscles, provided the bulk of the muscle was thoroughly explored by inserting the electrode at a number of positions and to a variety of

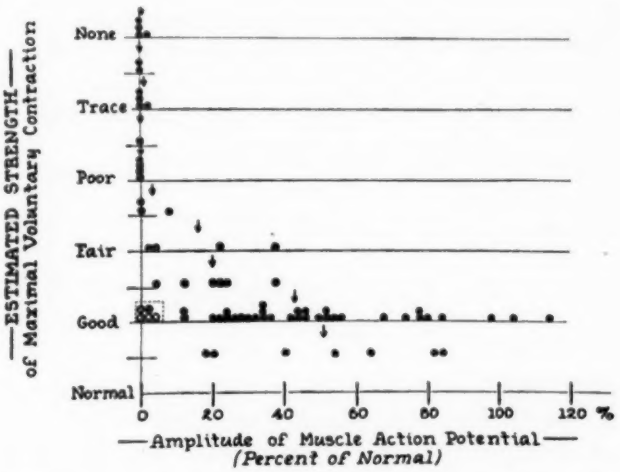

Fig. 7.—Relation between the estimated strength of maximal voluntary contraction and the amplitude of muscle action potential. Amplitude is expressed as a percentage of the amplitude for the corresponding muscle in the normal extremity of the same subject. (Arrows indicate the average amplitude for each group.) The categories of muscle strength are defined as follows: *None* is defined as no contraction detectable on palpation or careful observation of the skin overlying the muscle or its tendon; *Trace* as muscular activity detectable, but insufficient to cause movement of a joint, even when such movement is altogether unopposed; *Poor,* as tension sufficient to cause movement, but not when opposed by gravity; *Fair,* as movement when opposed by gravity, but easily resisted by the examiner, and *Good,* as movement accomplished against resistance offered by the examiner, but strength less than in the normal extremity. Some points (in the upper half of each horizontal division) have been placed in intermediate categories. In no case was muscle strength considered strictly "normal" after nerve injury, but seven muscles (lowest points) were rated as "good to normal."

depths, particularly near the point of entry of the nerve [13]; this, however, did not appeal to us as a procedure for extensive application.

13. Weddell, G.; Feinstein, B., and Pattle, R. E.: The Clinical Application of Electromyography, Lancet **1**:236-239, 1943; Electrical Activity of Voluntary Muscle in Man Under Normal and Pathological Conditions, Brain **67**:178-257, 1944.

Moreover, the method which we have used should provide a more quantitative index, even though it cannot be recommended as the most sensitive indicator of the first traces of recovery.

It is particularly difficult to explain a few cases in which mechanical strength was estimated as "good" but in which only very small potentials, or none at all, could be found. The five smallest action potentials included in the category of "good" mechanical strength are represented by points enclosed in the dotted rectangle in figure 7. Four of these, indicated by unfilled circles, were derived from the same patient at two different examinations of the abductor digiti quinti muscle and the first dorsal interosseous muscle. There was no known reason that the action potentials of this man should have exhibited exceptions to the relations found for other subjects. Unfortunately, he was not available for further examination. The other point included in the dotted rectangle (the filled circle) is for a muscle in another patient whose strength was rated as only "fair" on reexamination three weeks later; so possibly it was overrated at the first examination.

The wide range of amplitudes found for muscles with "good" strength is not surprising in view of the definition adopted for this category, according to which the degree of resistance offered by the examiner is undefined. In addition, it is possible that some of the patients with normal, or nearly normal, action potentials in response to nerve stimulation have not yet regained the ability to make full voluntary use of all the innervation available to them.

In concluding this section, we may well emphasize once again that the electromyographic technic employed here has an advantage over other methods of testing muscular recovery in that it does not rely on the cooperation of the patient. This is of value not only in cases in which the cooperative patient is unable to exercise equal volition with regard to his normal and his injured extremity, but also, occasionally, in assisting diagnosis in cases of suspected hysteria or malingering. Instances of the latter conditions will be considered in a later section.

TIME COURSE OF RECOVERY AFTER NERVE INJURY

The changes observed in the muscle action potential after nerve injury have been illustrated and described in the preceding section. In the present section, the data for all patients will be presented collectively in order to indicate the rates of recovery to be expected (*a*) in nerves after suture and (*b*) in nerves which recover without operation. For the collective presentation of results, it has been convenient to plot recovery, not simply as a function of time since injury, but, rather, as the time divided by the distance along the nerve from the lesion to the muscle. This procedure reduces the time scale in proportion to the distance the nerve fibers have to grow. If it happened that axons in different nerves

all grew at identical and constant rates, the recovery curves would coincide on such a plot, regardless of the level of the lesion. Therefore, deviations from the average rate of regeneration can more readily be detected.

No allowance has been made in our calculations for delay of growth across a suture or other injury or for the reestablishment of functional connections after the axon tips reach the muscle. We had no way of determining these factors from our own data, and no other estimates were available for man. The consistency of results was not improved by assuming that there were delays of the magnitudes found in animal experiments.[12b]

Recovery of Amplitude of Action Potentials After Nerve Suture.—The time course of recovery of the muscle action potential is shown

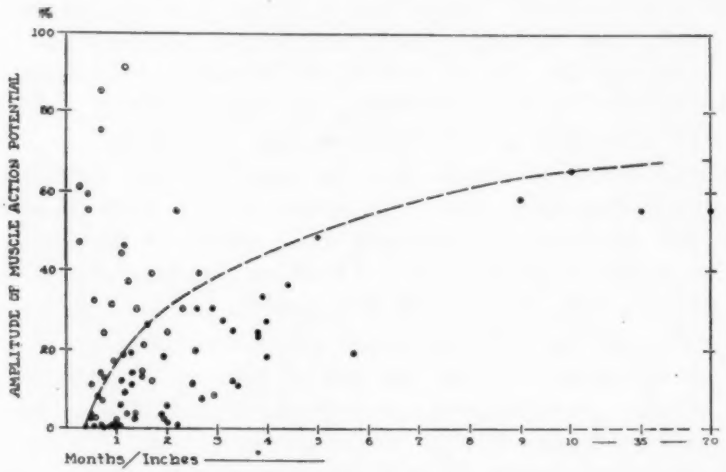

Fig. 8.—Amplitudes of muscle action potentials in various stages of recovery after nerve suture (indicated by solid black circles) and during recovery without operation on the nerve (hollow circles). The amplitudes (expressed as percentage of amplitude for the corresponding muscle in the normal extremity of the same patient) are plotted against the number of months allowed for recovery divided by the number of inches along the nerve from the injury to the active recording electrode. The number of months since operation was employed for the cases of suture, and since injury for cases of recovery without surgical repair of the nerve. All values for cases of suture appear below the broken line, whereas many spontaneous recoveries occurred much more rapidly. The scale of the abscissas has been compressed at the extreme right.

in figure 8. The cases of suture are represented by filled circles, all of which lie below the broken line.

The most rapid growth of motor axons which we have observed after suture occurred in a case in which a small muscle action potential was detectable 8 inches (20.5 cm.) below a suture which had been performed 3.3 months before, indicating a growth rate of 2.4 inches per month. In all other cases growth was slower, but in every instance the

leading axons grew at least 1 inch (2.5 cm.) per month. Thus, our data indicate rates of growth between 1 and 2.4 inches (2.5 and 6.0 cm.) per month, in good agreement with the commonly accepted figures of 1.2 to 2.4 inches (3 to 6 cm.) per month (1 to 2 mm. per day). A similar range was recently found by Seddon, Medawar and Smith [14] in observations on the time of reappearance of voluntary contraction in human muscles at various distances from a suture, indicating growth in the radial nerve of from 1.2 to 2.8 inches (3 to 7 cm.) per month (1.0 to 2.4 mm. per day).

It is important to recognize that the rates of recovery stated in the preceding paragraphs cover only the few most rapidly growing fibers, since they are calculated from the minimal detectable activity. Axons in sufficient number to contribute a functionally important quantity of innervation reestablish their peripheral connections much more slowly. This is indicated by the broken line in figure 8, which represents, as nearly as we could determine, the fastest observed rate of recovery after suture. For example, 30 per cent of the normal action potential was never attained in less than two months per inch of growth. Still longer times were required to reach greater degrees of function.

There is reason to doubt that the muscle action potential ever returns completely to normal after nerve suture. Our limited data suggest that the amplitude increases more slowly in the later stages than in the earlier stages of recovery. Moreover, the amplitudes of action potentials were only 55 per cent of normal in the hand muscles of a patient examined nearly twelve years after his ulnar nerve had been sutured at the wrist, the operation having been performed the day of injury. Such imperfect recovery is not surprising in view of the histologic changes that appear in denervated muscle [15] and the recognized misdirection of many nerve fibers during regeneration across a suture.[12c]

Data from figure 8, concerning the rate of recovery after suture, are replotted in figure 9, using distinctive symbols for different nerves. In addition, the points concerning each subject are connected by solid and broken lines. There is evidently no consistent difference between the regenerative capacities of the various nerves, since both the fastest and the slowest recoveries were observed among cases of suture of the ulnar nerve. Obviously, we have insufficient data to determine whether differences in rate of growth would appear in the averages of large numbers of cases.

Recovery of Amplitude of Action Potentials Without Nerve Suture.—A number of patients were studied who were recovering without nerve

14. Seddon, H. J.; Medawar, P. B., and Smith, R.: Rate of Regeneration of Peripheral Nerves in Man, J. Physiol. **102**:191-215, 1943.

15. Tower, S. S.: The Reaction of Muscle to Denervation, Physiol. Rev. **19**: 1-48, 1939.

suture from complete paralysis following battle injury. In order to limit this section to cases in which the paralysis was due to trauma, and not to hysteria, we included only (*a*) those patients in whom there was initial complete loss not only of motor, but also of sensory, function, with appropriate distribution, as ascertained from the case history or from the patient's own statement, and (*b*) those for whom the action potential in the more distal muscles was very small when first tested.

The results, represented by unfilled circles in figure 8, illustrate the well known fact that recovery is frequently much faster when occurring spontaneously than when suture of the nerve has been performed. We should like to emphasize that most, if not all, of the spontaneous recoveries included in this graph appear to have been due to a downgrowth of axons from the point of injury, rather than to gradual relief of a

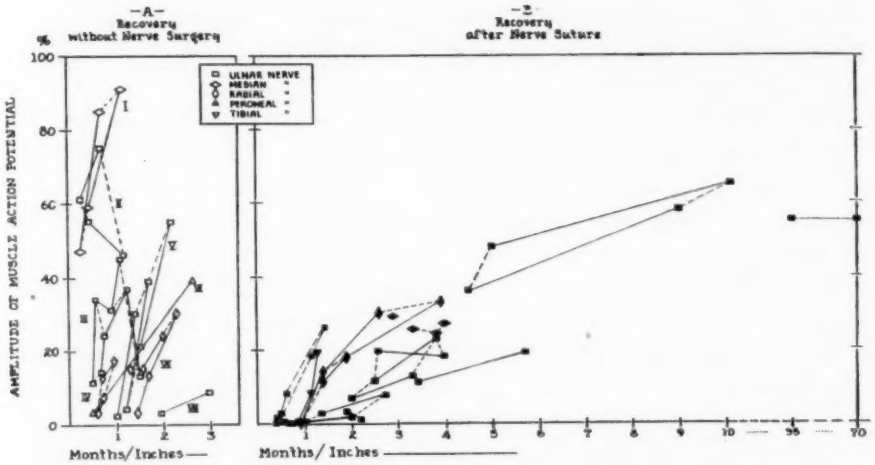

Fig. 9.—Data of figure 8 replotted to show additional details. Data on patients recovering without nerve suture are shown in *A*; those for patients requiring nerve suture, in *B*. Coordinates are the same as those in figure 8. Different nerves are represented by distinctive symbols, as indicated in the key. Solid lines connect measurements made on different muscles of one subject on the same day, while repeated observations on the same muscle are connected by broken lines. The scale of the abscissas has been compressed at the extreme right of *B*.

transient block of conduction which had not caused degeneration. This conclusion is based on the fact that at the time of our examination the proximal muscles and parts of muscles were in most instances much more fully recovered than the distal ones. This is indicated by the steep functional gradients shown in most cases by the solid lines connecting points for muscles tested on the same day in figure 9 *A*. Thus, under suitable conditions, human axons can regenerate much more rapidly than they are ever able to do after nerve suture. The difference in some cases is much greater than one would expect from the average

comparable figures for animal nerves after crushing and after suturing.[12b] The suitable conditions for most rapid growth presumably occur in those cases of concussive injuries which just suffice to cause axonal degeneration, without gross anatomic derangement of the nerve.

Recovery of Conduction Velocity.—It was pointed out in a preceding section that the conduction velocity of a regenerating axon is directly proportional to its diameter, so that measurements of velocity yield information concerning axonal maturation. The velocity of the most rapidly conducting (and therefore the largest) motor axons in a regenerating nerve can be accurately measured by the method described earlier in this paper. This method requires stimulation at two different distances from the muscle; unfortunately, this was done only in the 4 cases reported in table 2. However, many other observations showed that the latency of response was always greater than normal long after suture, and sometimes after recovery without surgical repair of the nerve. Presumably, these persistent changes were due, at least in part, to a reduction in conduction velocity.

In those cases in which the injured nerve was stimulated at only one distance from the muscle, there was no way of calculating accurately the conduction velocity. We have found it useful, however, to make an approximate calculation by assuming that the increase in latency was due entirely to a slowing of velocity. This may not be altogether correct, since the small increase in residual latency suggested by the few observations in table 2 may have been due in part to an increased delay at the neuromuscular junction. The approximate calculation was made, neglecting these possible changes at the junction, by dividing the average normal latency of response by the latency in the injured extremity, after first subtracting from each figure the average normal residual latency for the particular muscle (table 2). This yielded an approximate value for conduction velocity as a percentage of the normal velocity.

An additional assumption was made in those cases in which stimulation was applied above the lesion, namely, that the conduction velocity was normal down to the injury. This is in agreement with the observation of Berry and associates [10] on regenerating nerves in the cat that "in most instances the central [to a suture] conduction velocity was in the range of maximum normal values."

For three nerves for which accurate determinations were available (table 2), the velocities calculated by this approximate method were lower by 10 to 30 per cent. This difference is not necessarily due entirely to error in method of calculation, for the accurate method measures velocity only between the two points of stimulation of the nerve trunk, whereas the approximate calculation from total latency is also influenced by changes in the finer terminal portions of the axons.

In figure 10 the calculated velocities are plotted as a percentage of normal against the number of months since suture (black symbols) or against months since injury in those cases in which no nerve suture was performed (open symbols). The cases in which no operation was performed are again limited to those in which it was believed that initially a complete loss of function occurred in the nerve being studied, ascertained as described in the previous section.

In the measurements made less than four months after suture (fig. 10) the calculated conduction velocities varied from 5 to 15 per cent of normal. It should be emphasized that even the most slowly conducting and smallest of these fibers had established functional connections (i.e., were able to excite muscle fibers), for our measurements were dependent on the muscle response.

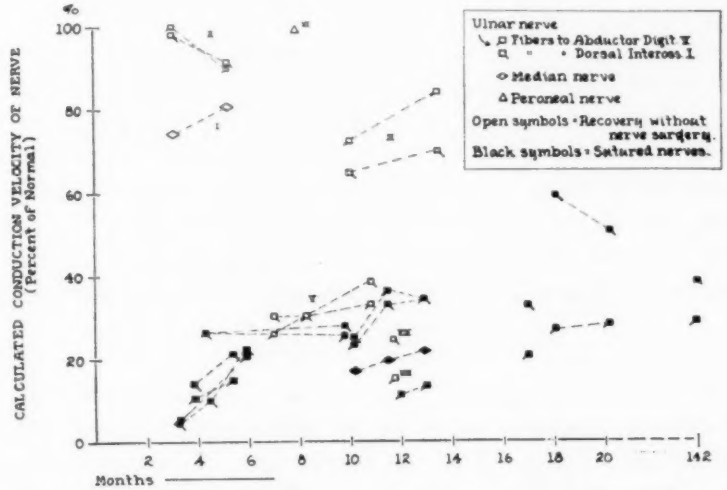

Fig. 10.—Approximate conduction velocities in regenerating nerves at various times after suture (black symbols) and at various times after injury for nerves not requiring operation (open symbols). The velocity (expressed as percentage of the average for a number of normal subjects) was calculated from the total latency, as described in the text. Roman numerals identify the cases of spontaneous recovery for which the amplitudes are recorded in figure 9. Repeated observations on nerve fibers supplying the same muscle are connected by dotted lines. The time scale has been compressed at the extreme right.

In later stages of recovery after suture the calculated conduction velocities were on the average higher than at first. However, in all the data presented in figure 10, the value exceeded 40 per cent of normal in only one sutured nerve, and the general impression gained from the plot is that the final degree of recovery is limited to about this value after suture. This suggests that the largest motor axons fail to grow beyond about 40 per cent of the diameter of the largest motor axons in normal nerve. This is a lesser limit to growth than that found by accurate measurement of velocities in the nerve trunk (up to 60 per cent of normal

in table 2). It has already been suggested the difference may be due to the fact that the present estimates include the finer terminal portions of the axons.

In striking contrast with the very slow, and probably never normal, maturation of axons after suture are the nearly normal conduction velocities calculated for several patients who did not require an operation on the nerve. In figure 10, it can be seen that after spontaneous recovery (open symbols) the velocities were from 65 to 100 per cent of normal in 4 injured nerves. There was evidence that the axons of 3 of these nerves had degenerated and were recovering by downgrowth from the point of injury, since the amplitudes of the muscle action potentials were much greater near the injury than more distally (nerves *I, III* and *VI,* figs. 9 and 10). A similar restoration to normal size has been found in animal nerves after degeneration produced by crushing (but not cutting) the nerve trunk.[16]

In 2 other cases of spontaneous recovery (*V* and *VIII,* fig. 10) the calculated conduction velocities seven to twelve months after injury were as slow as those after suture. It is significant that the start of recovery, as indicated by the action potential in the most distal muscles, was also more retarded in these nerves than in any other of the spontaneously recovering nerves for which velocity had been determined. Therefore, it is likely that the nerves were more seriously damaged in these 2 cases, resulting in conditions for growth comparable to those following suture.

HYSTERICAL PARALYSIS

In cases in which paralysis is suspected to be of hysterical origin, it is frequently simple to establish by electromyographic examination that the peripheral portions of the nerve trunk are altogether normal.[2] In figure 11 *A,* for example, are plotted the amplitudes of muscle action potentials recorded from a number of electrodes placed circumferentially around the normal and the affected arm of a patient with palsy of the radial nerve. In spite of the fact that this man claimed inability to extend the first three fingers of his left hand and could barely extend his wrist against gravity, there was no significant difference between the magnitude of muscle action potentials in his two arms. Thus, there can be no doubt that approximately the normal number of motor nerve fibers were able to function, at least below the point of stimulation. If there existed any true block to the passage of nerve impulses, it must have been more centrally located.

Another case of palsy of the radial nerve is illustrated by a similar plot in figure 11 *B.* Here, the action potentials recorded with electrodes placed over the brachioradialis muscle were quite normal, but there was

16. Gutmann, E., and Sanders, F. K.: Recovery of Fibre Numbers and Diameters in the Regeneration of Peripheral Nerves, J. Physiol. **101**:489-518, 1940.

possibly a deficit in the extensor muscles. Thus, there may have been a partial lesion in the deep radial nerve. There was, however, no deficiency great enough to explain the degree of weakness complained of by the patient, who was unable to extend his wrist when opposed by more than the very slightest resistance.

In table 4 are presented the findings in a third patient, who was apparently unable to produce more than a very slight motion of his ankle or to initiate any contraction of the muscles in his foot. Here, again, it is apparent that nerve function was not significantly impaired below the point at which the testing stimuli were applied near the knee. No importance could be attached to the apparent sizable deficit on the

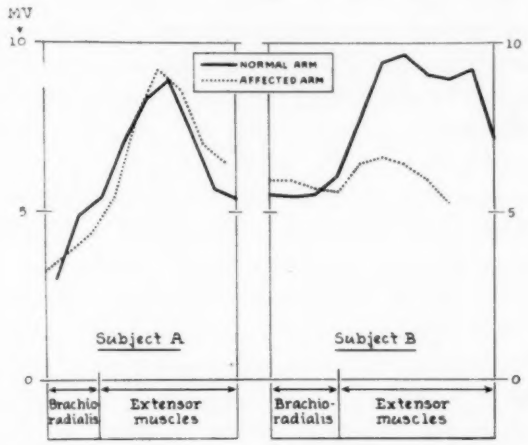

Fig. 11.—Distribution of action potentials around the forearm of 2 patients with a condition diagnosed as palsy of the radial nerve of hysterical origin. The amplitudes of responses to supramaximal stimulation of the radial nerve were measured through a number of electrodes equally spaced around the forearm 4 inches (10 cm.) below the olecranon. In subject *A* there was no detectable difference between the amplitude in the normal and that in the affected arm. In *B* the difference was not great enough to account for the degree of paralysis.

TABLE 4.—*Muscle Action Potentials as Percentage of Normal in a Case of Paralysis Diagnosed as Hysterical*

Nerve stimulated	Tibial	Peroneal
Action potential of leg muscles	120	94
Action potential of foot muscles	92	66

dorsum of the foot on stimulation of the peroneal nerve, in view of the other approximately normal figures, at least without repeated tests.

In discussing these examinations, we have purposely limited our conclusions to the state of the peripheral portions of the motor nerve fibers. Certainly, nothing can be said of the fibers central to the point of stimulation, except that at the time of examination they were not

injured sufficiently to cause wallerian degeneration. In addition, it is presumably safe to assume that a normal muscle action potential indicates that the muscle is able to contract, for we are not aware of any condition which impairs the contracting mechanism but not the action potential.

SUMMARY

Muscle action potentials in response to supramaximal percutaneous stimulation of various nerves were recorded in a number of normal subjects, in patients with peripheral nerve injuries and in a few persons with a condition diagnosed as hysterical paralysis. The potentials were recorded through small electrodes on the skin. Convenient electrodes and supports were devised for recording from all the major muscle groups in the forearm, hand, leg and foot. Control observations were made to determine the limitations of the method, particularly those due to the wide spread of the action potential of each muscle. Decrease in amplitude of the action potential after nerve injury indicated decrease in the number of muscle fibers innervated, while increase in latency of the response indicated slowing of the conduction velocity of the regenerating nerve fibers and, therefore, a decrease in axonal diameter.

The normal conduction velocities of the fastest nerve fibers supplying the intrinsic muscles of the hand and foot ranged from 46 to 67 meters per second. During recovery following nerve suture, and sometimes during spontaneous recovery of nerve function, the velocities were much lower, being accurately measured at less than 50 per cent of normal in some cases and estimated to be as low as 5 to 10 per cent of normal in others. Velocity increased progressively during the first year after suture, but probably never regained more than 60 per cent of normal. Since velocity is known to be directly proportional to the diameter of an axon, this implies a similar limitation in axonal growth after suture. In contrast, fibers of approximately normal velocity were found in several cases in which regeneration occurred without operation on the nerve.

The amplitude of action potential recorded from a given normal muscle was variable (average difference between duplicate determinations, 23 per cent) ; in addition, the average amplitude was different for different muscles. In examination of muscles the nerves of which had been injured, the amplitude of the maximal response was therefore routinely expressed as a percentage of the maximal action potential of the corresponding muscle in the uninjured extremity of the same subject.

After nerve suture, muscle action potentials in response to stimulation of the nerve were first detectable at a time which depended on the distance from the lesion to the muscle. The values indicated rates of regeneration in good agreement with the commonly accepted rates

of 1 to 2 mm. per day. In general, reinnervation could be detected before an action potential could be recognized by watching for movement during a voluntary effort of the patient.

For the later stages of recovery, it was convenient to plot the percentage of the normal amplitude of action potential against the number of months allowed for recovery divided by the distance from the lesion to the muscle. Against this abscissa, recovery was found to occur at more or less comparable rates in various sutured nerves. In comparison, those nerves which did not require operation recovered their function at a wide variety of rates, often much more rapidly than after the most favorable suture. By comparison with data such as these, it should be possible to tell whether recovery is lagging unduly in any case of peripheral nerve injury in which a similar electromyographic examination is made.

In cases of hysteria or malingering the normality of the peripheral nerve and muscle could be definitely demonstrated.

Miss Edna Hill prepared the graphs and Mr. Warren Founds made the photographic reproductions.

Johnson Research Foundation, University of Pennsylvania (Dr. Hodes and Dr. Larrabee).

Department of Surgery, Yale University School of Medicine (Dr. German).

CHANGES IN THE BRAIN ASSOCIATED WITH ELECTRONARCOSIS

Report of a Case

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THE USE of a prolonged electric current applied to the brain to produce a narcosis-like state, as a form of psychiatric treatment, was introduced by Frostig and associates [1] in 1944. That a unidirectional pulse current could produce such a narcotized condition was first shown by Leduc in 1902, with rabbits and dogs and in experiments on himself.[2] His observation was confirmed by others, and this form of narcosis was tried as a means of anesthesia, with some success.[3]

In 1942, van Harreveld and associates [4] experimented with various types of current capable of inducing electronarcosis and concluded that the state could be produced with a variety of frequencies of both pulsating and alternating currents. They stated that the narcosis is due to the stimulating properties of the current applied and added confirmatory evidence in a later paper.[5] Frostig made this a point of fundamental differentiation between chemical and electrical narcosis.

The procedure is defined as a prolonged application of electric current to the brain, producing a controlled state of unconsciousness, preceded by a modified convulsion.[6] It consists essentially in giving

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From the Department of Neurology, Jefferson Medical College.

1. Frostig, J. P.; van Harreveld, A.; Reznick, S.; Tyler, D. B., and Wiersma, C. A. G.: Electronarcosis in Animals and Man, Arch. Neurol. & Psychiat. **51**: 232-242 (March) 1944.

2. Leduc, S.: Production du sommeil et de l'anesthésie générale et locale par les courants électriques, Compt. rend. Acad. d. sc. **135**:199-200 and 878-879, 1902.

3. LeClerc, G.: L'anesthésie électrique chez l'homme Cong. franç de chir. **23**:665, 1910.

4. van Harreveld, A.; Plesset, M. S., and Wiersma, C. A. G.: The Relation Between the Physical Properties of Electric Currents and Their Electronarcotic Action, Am. J. Physiol. **137**:39-46, 1942.

5. van Harreveld, A.; Tyler, D. B., and Wiersma, C. A. G.: Brain Metabolism During Electronarcosis, Am. J. Physiol. **139**:171-177, 1943.

6. Tietz, E. S.; Thompson, G. N.; van Harreveld, A., and Wiersma, C. A. G.: Electronarcosis: Its Application and Therapeutic Effect in Schizophrenia, J. Nerv. & Ment. Dis. **103**:144-163, 1946.

an initial large dose of current, in a manner similar to that used in standard electric shock, and then stepping the current down and maintaining it at a lower level, with slight variations, for the length of the desired narcosis. A standard procedure for this therapy was fully described by Tietz and co-workers.[6] The reactions during the treatment were described as follows:

> When the current is first applied at the customary initial dose of 160 milliamperes, there is usually an immediate tonic flexion of the extremities, followed, after 10-15 seconds, by extension, at least of the legs. There is an initial short cardiac arrest, after which the heart beats slowly and often irregularly. The face and often the neck and chest become flushed during this period. After 30 seconds the high initial current is rapidly lowered to from 60 to 70 milliamperes. The tonic contraction relaxes and is replaced by clonic twitches of weak to moderate intensity. These movements are usually over in 10 seconds. Respiration starts with a deep gasp after 45 to 60 seconds of current. With slight adjustments of dose, this state of electronarcosis, in which the patient is quiet but has developed considerable flexor tone in the arms and extensor tone in the legs, is maintained for 7 minutes.[6]

This form of therapy was apparently introduced as a substitute for insulin in the treatment of schizophrenia, being less costly, less time consuming and simpler to administer.[7] Thompson and associates[8] used electronarcosis in the treatment of 50 schizophrenic patients and concluded that it compares favorably with insulin shocks and is better than the standard electric shock.

Frostig and associates[1] reported the deaths of 2 dogs which were given experimental electronarcosis and stated that death was probably caused by heart failure, due to the unusual effort demanded of the heart during the hyperkinetic period. This violently hyperkinetic reaction is not seen in human subjects. Globus and associates[9] studied the brains of 7 dogs subjected to this form of therapy and found no pathologic alterations. One of the animals, after receiving the usual treatment, was electrocuted, and its brain showed no histologic changes. No serious complications have been recorded as a result of this treatment in human subjects. Tietz and associates,[6] after administering 1,400 treatments, reported 1 case of compressed fracture of a thoracic vertebra.

We have recently had the opportunity to study the brain of a patient who died three hours after a single treatment with electronarcosis. The results of the histopathologic studies of this brain are reported here.

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7. Tietz, E. B.; Thompson, G. N.; van Harreveld, A., and Wiersma, C. A. G.: Electronarcosis: A Therapy in Schizophrenia, Am. J. Psychiat. **101**:821-823, 1945.

8. Thompson, G. N.; McGuinis, J. E.; van Harreveld, A.; Wiersma, C. A. G., and Tietz, E. B.: Electronarcosis, War Med. **6**:158-161 (Sept.) 1944.

9. Globus, J. H.; van Harreveld, A., and Wiersma, C. A. G.: The Influence of Electric Current Application on the Structure of the Brain of Dogs, J. Neuropath. & Exper. Neurol. **2**:263-276, 1943.

REPORT OF CASE

History.—E. B., a white woman aged 28, was first admitted to the New Jersey State Hospital on Oct. 27, 1927, at the age of 9 years because of mental deficiency and obstreperous behavior. She had been born out of wedlock and adopted into a

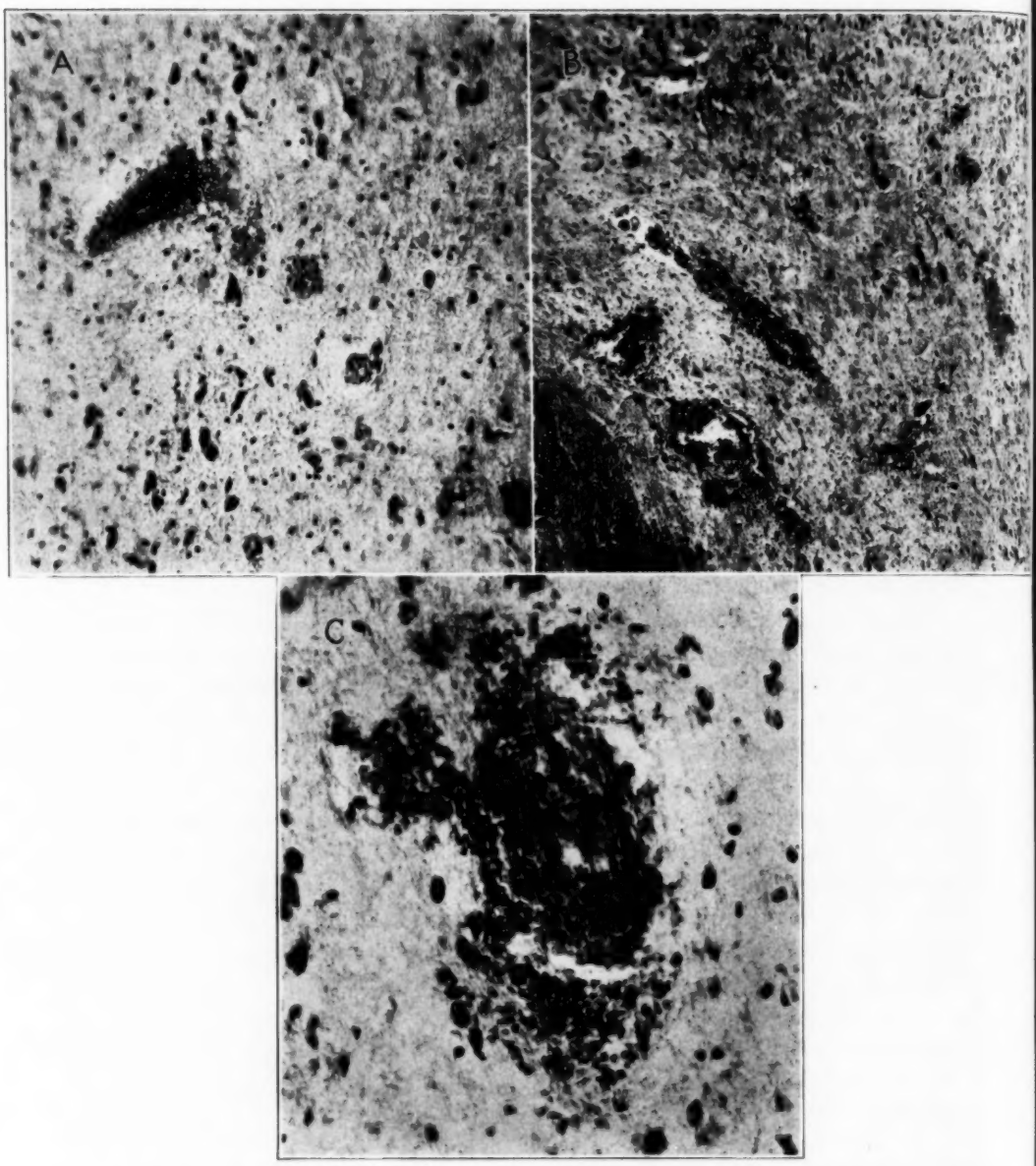

Fig. 1.—*A*, hemorrhages in the hypothalamus above the supraoptic nucleus; *B*, hemorrhages in the hypothalamus in the region of the fornix; *C*, higher power of one of the hemorrhages, showing the fresh, noncrenated red cells.

private home at the age of 13 months, but she early exhibited signs of retardation and became a difficult behavior problem. She was transferred to the Vineland

State School on March 8, 1928, but was vicious, assaultive, unclean and obscene; she was returned to the New Jersey State Hospital, where she remained until her death.

On readmission, she weighed 70 pounds (31.8 Kg.) and was 4 feet 7 inches (139.7 cm.) tall. Physical examination, including routine studies of the blood, gave results entirely within normal limits. In the hospital the patient was excitable, destructive, assaultive, mischievous, impudent and exhibitionistic. Her mental ability could not be determined accurately, but she was obviously defective; and the diagnosis was manic-depressive psychosis, manic type, with mental deficiency. She

Fig. 2.—Hemorrhage in the cerebellum with hemosiderin-laden phagocytic cells.

persisted in this behavior despite several attempts at therapy, including injections of killed typhoid bacilli, colonic irrigations and malaria. On Sept. 15, 1941 a course of electric shock therapy was begun and was completed July 8, 1942; but the response was not satisfactory, and she continued to require constant observation and frequent isolation. Repeated physical examinations throughout these years revealed no abnormalities.

Electronarcosis Therapy.—On Sept. 20, 1946 it was decided to give her a course of electronarcosis therapy. She was then 28 years of age. Because of her extreme restlessness, she was given morphine sulfate, ¼ grain (16 mg.), and scopolamine hydrobromide, 1/150 grain (0.4 mg.), one-half hour before the treatment. The electrodes were placed in the usual bitemporofrontal position; a

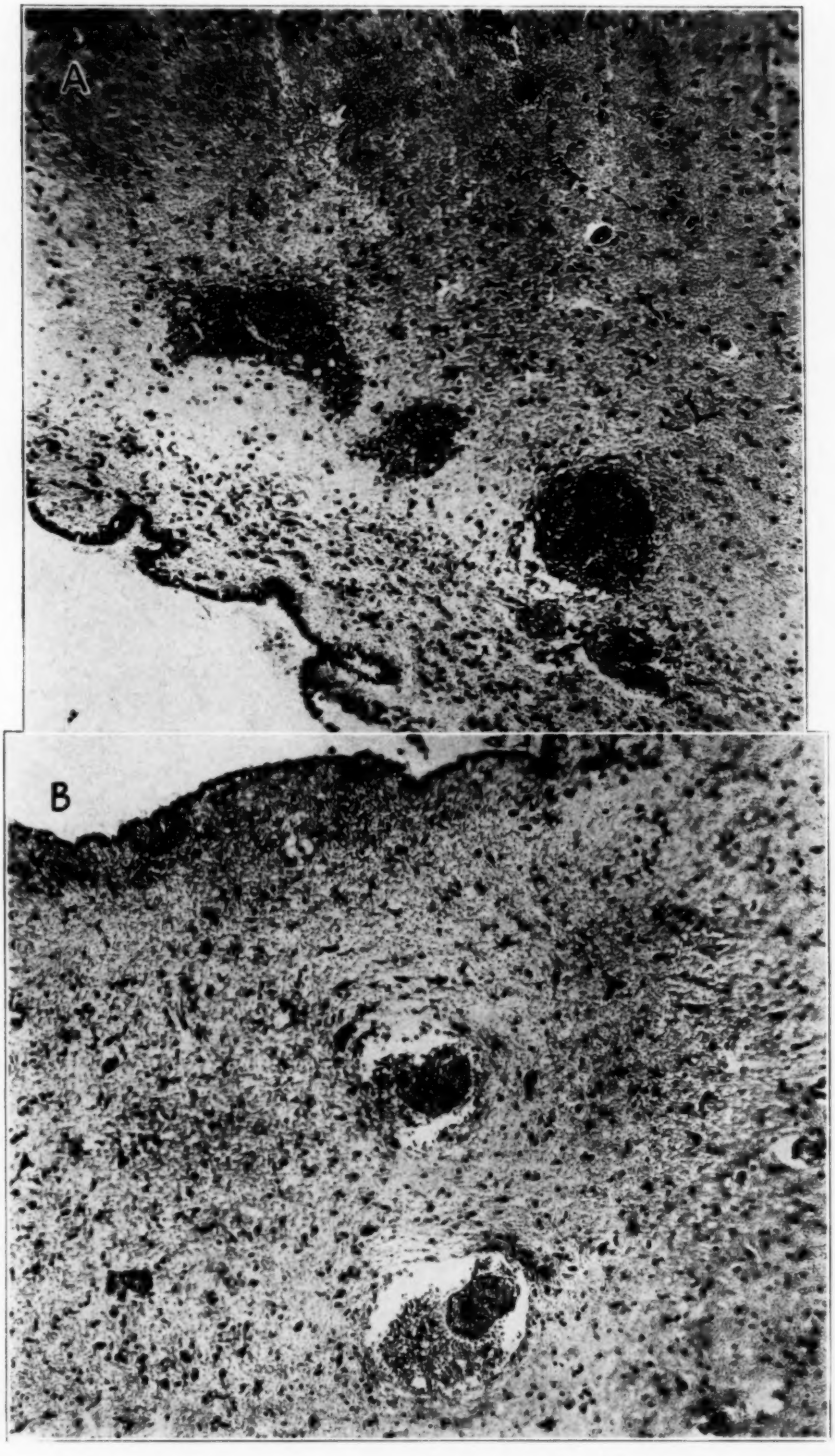

Fig. 3.—Hemorrhages (*A*) in the caudate nucleus and (*B*) in the medial nucleus of the thalamus.

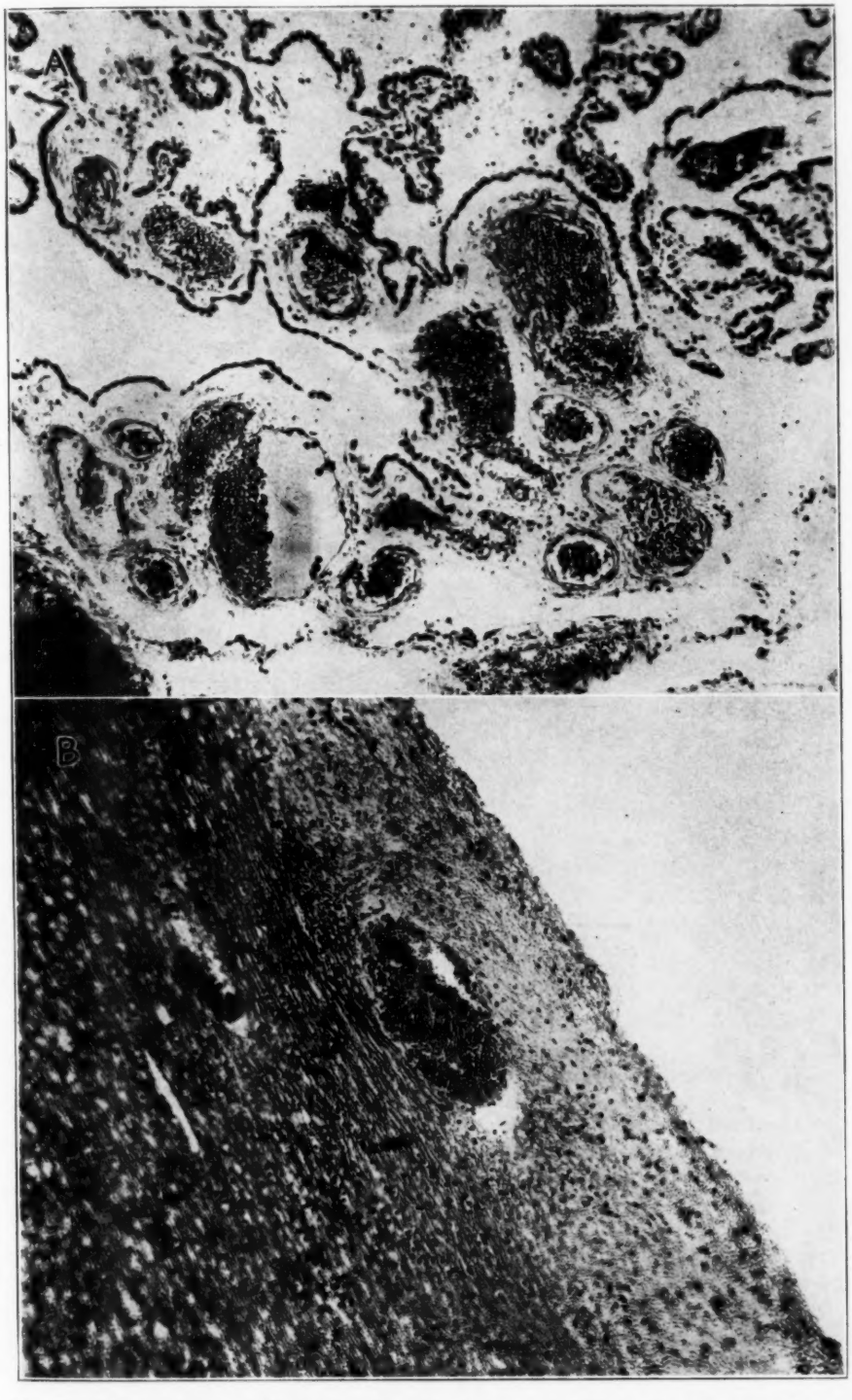

Fig. 4.—Hemorrhages (*A*) in the choroid plexus and (*B*) in the corpus callosum.

current of 180 milliamperes and 100 to 200 volts was used. She was given three bursts of ten seconds each over a period of one minute. She became tonic, remaining so until the current was shut off, when she relaxed. One hour after the treatment, she responded to external stimuli by opening her eyes, but she continued in what appeared to be deep sleep until she died, three hours after administration of the current. There were no unusual or warning features suggesting her critical state in this three hour interval, or even at the time of her death.

Necropsy.—The general pathologic examination was reported as showing nothing abnormal. Grossly, the brain appeared normal except that the convolutions

Fig. 5.—Hemorrhage in the parietal lobe of the cerebral cortex.

were somewhat flattened. The meninges over the vertex were clear and translucent. Pial vessels were engorged, but the vessels at the base were normal. Coronal sections of the cerebrum revealed no gross abnormalities of the cortical gray matter, the centrum semiovale, the basal ganglia or the ventricular system. Cross sections of the brain stem and cerebellum showed no gross lesion.

Microscopic examination revealed that the leptomeninges had undergone fibrous thickening and contained a small number of fresh, noncrenated red cells, scattered throughout the subarachnoid space. The blood vessels of the meninges were greatly dilated and engorged. Throughout the cortical gray matter, the ganglion cell population was decreased in distinct areas, and many of the remaining cells showed chromatolysis and eccentrically placed nuclei. Shadow cells were numerous. Many of the small arterioles showed moderate proliferative changes in

the intima. No other alterations were apparent in the frontal or motor region. Sections through the parietal lobe revealed many petechial hemorrhages, composed of fresh, noncrenated red cells and small amounts of hemosiderin. These hemorrhages occurred only in the gray matter, most frequently in laminas 1, 2 and 3. In the temporal region there was one small hemorrhage near the surface, with well formed red cells and no hemosiderin. No hemorrhages were observed in the occipital lobes, but considerable laking of blood was evident in the meningeal vessels. The white matter was normal throughout.

Fig. 6.—Hemorrhage in the optic tract.

In the body of the corpus callosum, at the level of the head of the caudate nucleus, were several fresh hemorrhages. Similar lesions were seen in the optic tract at the level of the decussation and in the pineal gland. Larger hemorrhages, also fresh, with the red cells in various states of dissolution, were observed in the heads of the caudate nuclei, the medial nucleus of the thalamus, the posterior hypothalamic nuclei bilaterally, the supraoptic nucleus, the choroid plexus of the lateral ventricles and the inferomedial portion of the cerebellum in the superficial molecular layer, at the level of the hypoglossal nucleus. These larger lesions consisted in extravasated blood surrounding the blood vessels in some instances,

the vessels being destroyed in others. Hemosiderin and phagocytic activity could be seen in these hemorrhages, but there was no increase in glial cells surrounding them.

No lesions were apparent in the medulla or the pons. Throughout the brain there were pronounced vascular dilatation and engorgement, with frequent slight perivascular extravasations, the red cells appearing well formed. Stains for myelin sheaths showed no alterations in the region of the hemorrhages or elsewhere.

COMMENT

Prior to this time, there have been no recorded fatalities in electronarcosis treatment. The patient reported in this paper died three hours after her first electronarcosis treatment. Histopathologic study of the brain revealed scattered hemorrhages, engorgement and dilatation of the blood vessels and loss of ganglion cells. The larger, more distinct hemorrhages were seen in the head of the caudate nucleus, the medial nucleus of the thalamus, the posterior hypothalamic nucleus, the supraoptic nucleus, the cerebellum and the choroid plexus of the lateral ventricles. These were all recent, but some hemosiderin and phagocytic activity were present. There were smaller, fresh hemorrhages in the superficial layers of the gray matter of the parietal and temporal lobes, the corpus callosum, the optic tract and the pineal gland.

The areas of decreased ganglion cell population were compatible with the mental deficiency manifested by the patient and were of long standing. The other changes, however, must be considered as directly or indirectly related to the treatment. The hemorrhages were very recent, corresponding with the time factors involved. It is not possible to implicate any of the other forms of treatment, for the patient's last intensive course of therapy, consisting in electric shock, was received in 1942, at least four years prior to her death. It is improbable that the sedatives given before the treatment were responsible, as the dose was small; moreover, the electric current has a stimulating effect, which should counteract any depressive action the drug might have. Tietz and associates even recommended the intravenous administration of "sodium amytal" in the case of resistive patients, as described by Impastato and associates.[10] Finally, the general pathologic examination revealed nothing else to account for the changes.

These lesions were more definite than the reported changes in the brain associated with standard electric shock.[11] They were somewhat similar in type and distribution to those in the first case described by

10. Impastato, D. J.; Bak, R.; Frosch, J., and Wortis, S. B.. Modification of the Electrofit, Am. J. Psychiat. **100**:358-360, 1943.

11. Alpers, B. J.: The Brain Changes Associated with Electric Shock Treatment: A Critical Review, Journal-Lancet **66**:363-369, 1946.

Alpers and Hughes,[12] in which hemorrhages of small size and varying age were scattered throughout the brain. In the present case the hemorrhages were larger and more distinct, especially in the hypothalamic and caudate nuclei.

In view of the experimental studies (Globus) showing that electronarcosis does not produce damage to the brain, it seems hazardous to suggest that the changes in the brain, notably the hemorrhages, were related to the treatment. The method has been used clinically without ill effect (Tietz). Nevertheless, it may reasonably be assumed that in our case the hemorrhages were related to the treatment. Whether they were the direct result of application of the electric current, or whether they were agonal, is immaterial in this case, since in either event the treatment itself was implicated. It would be inaccurate to assert that electronarcosis is associated with damage to the brain, but it is desirable, nonetheless, to record a case of death following this treatment.

SUMMARY

The pathologic changes in the brain of a patient who died three hours after the first treatment with electronarcosis are reported.

1. There were distinct, recent hemorrhages in the caudate nuclei, the medial nucleus of the thalamus, the posterior hypothalamic nuclei, the supraoptic nucleus, the cerebellum and the choroid plexus of the lateral ventricles.

2. There were fresh, smaller hemorrhages in the cerebral cortex, the corpus callosum, the optic tract and the pineal gland.

These changes must be considered related to the treatment, in view of the time relation, the nature of the lesions and the absence of any other probable causative agent.

Jefferson Medical College.

12. Alpers, B. J., and Hughes, J.: Brain Changes in Electrically Induced Convulsions in Humans, J. Neuropath. & Exper. Neurol. **1**:173-180 (April) 1942.

THE ELECTROENCEPHALOGRAM OF MULTIPLE SCLEROSIS

Review of the Literature and Analysis of Thirty-Four Cases

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MULTIPLE sclerosis, according to Grinker,[1] ranks third in frequency among neurologic disorders. Its incidence varies somewhat with geographic location, and apparently with other factors, for Wilson [2] stated that between 1908 and 1925 at the National Hospital it actually ranked first (multiple sclerosis, 1,398 cases; intracranial tumor, 1,352 cases; neurosyphilis, 1,340 cases), while the average occurrence in England and Wales over a long period was second only to that of neurosyphilis. In Switzerland [2] the disease is said to be twice as frequent as in England. Neilsen [3] stated that the disease has become much more frequent in the United States in the past fifteen years. Camp [4] has seen approximately 2,500 clinic cases and 700 private cases in the past forty years. In the University of Michigan Hospital the diagnosis of multiple sclerosis was made in 485 cases in the five year period ending March 31, 1947.

The literature on electroencephalography up to January 1947 includes approximately 1,300 references. Despite this enormous activity, only one article (Hoefer and Guttman [5]) is specifically and definitively devoted to the electroencephalogram of multiple sclerosis. This amazing disparity between the great frequency of this grave disease, on the one

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A dissertation submitted in partial fulfilment of the requirements for the degree of Master of Science in Neurology in the University of Michigan.

1. Grinker, R. R.: Neurology, ed. 3, Springfield, Ill., Charles C Thomas, Publisher, 1943.

2. Wilson, S. A. K.: Neurology, Baltimore, Williams & Wilkins Company, 1941.

3. Nielsen, J. M.: Textbook of Clinical Neurology, ed. 2, New York, Paul B. Hoeber, Inc., 1946.

4. Camp, C. D.: Personal communication to the author.

5. Hoefer, P. F. A., and Guttman, S. A.: The Electroencephalogram in Multiple Sclerosis, Tr. Am. Neurol. A. **70**:70, 1944.

hand, and its apparent neglect in the tremendous electroencephalographic literature, on the other, has prompted me to conduct a series of investigations on the correlation of the two. The first results of this study are embodied in this report.

REVIEW OF LITERATURE

There is a total of 6 references to the electroencephalogram in cases of multiple sclerosis. Berger [6] in 1931, stated that in cases with severe psychic changes the electroencephalogram was abnormal, whereas in cases without psychic changes the tracing was normal. He did not describe the type of abnormality, nor did he reproduce tracings of it. Lemere,[7] in 1936, mentioned 18 cases studied electroencephalographically. His study, unfortunately, was limited by the instrumental and technical inadequacies of that period of electroencephalography. He used two moist pad electrodes, 2 cm. in diameter, soaked in saline solution and applied to the forehead and the occiput. Despite these difficulties, he obtained some evidence of abnormality but apparently did not attach much significance to it. Of the 18 cases, he discarded the records of 5, as "there were signs of mental deterioration that invalidated the findings." It may well be that in these advanced cases with psychic disorganization he discarded valid electroencephalographic evidences of cortical or subcortical damage. Of the remaining 13 cases, "good" Berger (alpha) rhythm was present in 5, in contrast to the remainder of the group, in which there were average or "poor" rhythms. His picture of "good" Berger rhythm is one of moderate voltage, 10 per second waves. The picture of "poor" rhythm is one of low voltage, 12 to 20 per second waves with an occasional positive, cone-shaped discharge or diphasic spike formation. No slow wave formations were evident. Gibbs and Gibbs,[8] in their monumental "Atlas of Electroencephalography," state: "Patients with multiple sclerosis and evidence of cortical involvement may show scattered slow waves (6 to 8 p. s.) (Berger, 1931) but many severe cases of this disease have no EEG evidence of disorder." They show three tracings. The first presents "fairly continuous 9 to 10 p. s. activity with scattered 7 to 8 p. s. waves showing best in the occipital lead. This much 7 to 8 p. s. activity in an adult is considered questionably normal." The second tracing is described as "continuous 10 p. s. activity in all leads, lowest voltage in

6. Berger, H.: Ueber das Elektrenkephalogramm des Menchen, Arch. f. Psychiat. **94**:16, 1931.

7. Lemere, F.: The Significance of Individual Differences in the Berger Rhythm, Brain **59**:366, 1936.

8. Gibbs, F. A., and Gibbs, E. L.: Atlas of Electroencephalography, Cambridge, Mass., Lew A. Cummings Co., 1941.

frontal leads. Normal record." The last record bears the notation, "almost continuous 9 to 10 p. s. activity in all leads. Lowest voltage in frontal. Normal record." There is no specific mention of whether the monopolar or the bipolar technic was used, nor is the site of electrode placement described, although it may be assumed that the records were obtained with the standard technic described earlier in their text. Freeman,[9] in 1944, reported 15 cases of multiple sclerosis; pneumoencephalographic studies were made in 13 of these, electroencephalographic studies in 6 and both pneumoencephalographic and electroencephalographic studies in 4. He reported that the electroencephalogram was substantially normal in all but 1 case, in which high voltage 2 to 5 per second waves were found during an acute exacerbation. This slow wave activity disappeared during remission. Freeman's paper was chiefly concerned with the pneumoencephalographic changes, and he interpreted the "cortical atrophy" of other investigators as merely the sinking in of the unharmed cortex by virtue of the cicatricial contraction of the subcortical white matter. He explained his electroencephalographic changes as follows:

> . . . the cellular constellations are continuing their activity unhampered by the loss of myelin sheaths in the subjacent tissue, or that 'dead cells like dead men, do not talk.' A third alternative, that the atrophic focus is too small to give rise to abnormal electrical impulses, is scarcely tenable, since positive electroencephalographic evidence of cortical dysrhythmia is very evident in certain cases of focal lesions that are considerably smaller than the large patch of subarachnoid air would seem to indicate.

In another paper, published two months later, Freeman and Cohn[10] presented what appears to be the same series of 15 cases, the emphasis again being on pneumoencephalography. The pneumoencephalogram revealed symmetric dilatation of the ventricles and irregular stellate shadows and large striations over the surface of the brain, occasionally symmetrically located. Increased air in the posterior fossa, especially around the pons, was seen in some cases. The fourth ventricle was dilated, and the cerebellar folia were prominent. In some cases pneumoencephalograms made at intervals showed increased enlargement of these air shadows, particularly in the third ventricle. In some cases of long duration the changes were minimal. Autopsy revealed destruction and cicatricial contraction of the subcortical white matter in 4 cases. These areas corresponded with the pneumoencephalographic shadows.

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9. Freeman, W.: Frontiers of Multiple Sclerosis, M. Ann. District of Columbia **13**:1, 1944.

10. Freeman, W., and Cohn, R.: Electroencephalographic and Pneumoencephalographic Studies of Multiple Sclerosis, Arch. Neurol. & Psychiat. **53**:246 (March) 1945.

Histologic examination showed destruction of subcortical white matter, with the cortex almost entirely unaffected except for the radial fibers. The authors concluded:

> . . . Pneumoencephalographic findings are due not to local cortical atrophy but to sinking in of the cortex following cicatricial contraction of the subcortical white matter, and . . . the electroencephalogram, which is normal [in multiple sclerosis], shows a high correlation with the preservation of architecture of the cerebral cortex. . . . The cell bodies themselves and the intact intracortical connections apparently keep up this wave pattern through the cortex.

The authors looked to the early work of Dusser de Barenne and McCulloch [11] for support of their contention that the action potentials are a function only of the cortex. In discussing this paper, Winkleman [12] stated: "Knowing, therefore, that the morbid process of multiple sclerosis is subcortical, and not cortical, one is not surprised to learn that there is little or no change in the electroencephalogram." These deductions concerning the pathoanatomic and electroencephalographic status will be discussed later.

The most recent, and only truly definitive, paper devoted to the electroencephalogram of multiple sclerosis (Hoefer and Guttman [5]) has previously been mentioned. They studied 107 cases of typical multiple sclerosis with a Grass six channel, ink-writing oscillograph. Sixteen electrodes (both bipolar and monopolar recording) were used. "Most patients were subjected to a five minute period of hyperventilation." These authors found normal records in 23.3 per cent of cases, essentially normal records in 32.7 per cent, diffusely abnormal records in 21.5 per cent and abnormal records with focal signs in 22.5 per cent. They thus obtained abnormal electroencephalographic records in 44.0 per cent of their cases. Repeated electroencephalographic recording in 10 cases revealed the tendency of focal or diffusely abnormal patterns to disappear with remission of the disease. The authors concluded that abnormal electroencephalograms occurred in a statistically significant number of cases (44.0 per cent) and that, therefore, it could be assumed either that the gray matter was involved in multiple sclerosis or that the function of the cortical axons was changed when large tracts in the white matter were involved in structural lesions.

METHOD AND MATERIAL

Of the 485 cases in which the diagnosis of multiple sclerosis was made during the five year period ending March 31, 1947, electroencephalograms were made in 44. The program is continuing and an attempt is being made to secure an electro-

11. Dusser de Barenne, J. C., and McCulloch, W. S.: Some Effects of Laminar Thermocoagulation upon the Local Action Potentials of the Cerebral Cortex of the Monkey, Am. J. Physiol. **114**:692, 1936.

12. Winkleman, N. W., in discussion on Freeman and Cohn.[10]

encephalogram on each patient seen in this clinic, so that the statistical significance of the ultimate findings may be validated by an adequate sampling of material. In addition, Dr. Carl D. Camp has given me permission to include his private cases in the final study.

The case histories were examined critically and cases were rejected unless they presented a textbook history and clinical picture of multiple sclerosis. Ten cases were excluded because they failed to meet these diagnostic requirements. The electroencephalograms in the remaining 34 cases were then analyzed. In all 34 cases the disease was in exacerbation at the time of the electrical recording. Most of the records were made with the Grass three channel, ink-writing oscillograph. A few were made with the six channel Grass apparatus. Ordinarily, ten electrode placements were made, but in cases in which focal signs appeared or the clinical record pointed to focal activity, additional electrodes were used, the total number varying from seventeen to twenty-six. Electrodes were of the flat lead disk type and were applied to the skin over a thin layer of electrode paste

TABLE 1.—*Minimum Recording Time for the Ten Electrode Technic*

Site	Recording Time, Min.	Site	Recording Time, Min.	Site	Recording Time, Min.
Right frontal Right motor Right occipital	3	Right motor-occipital Left motor-occipital Left motor-temporal	2	Left frontomotor Left motor-occipital Left occipitotemporal	2
Left frontal Left motor Left occipital	3	Right motor Left motor Right occipital	2	Right occipital Left occipital Right motor	2
Right frontomotor Left frontomotor Right motor-temporal	2	Right temporal-left temporal Right temporal Left temporal	2	Right occipital Left occipital Right motor	2 Hyperventilation
Right temporomotor Right motor-left motor Left motor-temporal	2	Right frontomotor Right motor-occipital Right occipitotemporal	2	Right occipital Left occipital Right motor	1½+ after hyperventilation

and fastened with collodion. Records for the most part were taken in an air-conditioned room. Most of the recordings were made by technicians, but a few were made by me.

The routine electrode placement included the frontal, upper motor, upper occipital and midtemporal regions and the ear lobe on each side. When more than ten electrodes were used, the excess number were symmetrically placed on the scalp between the routine electrodes. A record was made of all distances between electrodes, approximate anatomic landmarks being used as points of reference. The minimum recording time for the ten lead technic is given in table 1. When more than ten leads were used, the recording time was influenced by the findings.

Hyperventilation consisted in a two minute period of forced respiration, before which the patient was first instructed to breathe at the rate of about thirty inspirations and expirations per minute. During the taking of the record, the patient was told to breathe faster or deeper, as the circumstances required; and a pencil mark was made on the running tape at each inspiration, so that an evaluation of the frequency and depth of inspiration could be made when the record was reviewed.

STANDARDS OF INTERPRETATION

The interpretation of electroencephalographic tracings was in accordance with standards established by Bagchi and associates [13]; these standards are stated here verbatim, for the reason that they were presented only as an appendix to the reprints and therefore are not available in the literature.

The normal electroencephalograms include one or more of the following features:—the general frequency characteristic between 8½ and 12½ per second of regular or fairly regular sequences; or low voltage waves of an indefinite form (not sharp) 14 to 20 per second, with or without interspersing single slow waves less than 8½ per second and less than 10 per cent of the time, or inconspicuous sharp waves of 14 to 20 per second. The borderline record has several of the following features:—the general frequency characteristic between 8½ and 12½ per second with a great irregularity of the form of the waves; general frequency characteristic slightly less than 8½ per second; about 10 per cent of the waves less than 8½ per second as singles or as serials; about 10 per cent of 14 to 30 per second waves of a sharp character (with paper speed 30 millimeter per second) with a voltage of more than 15 microvolts; a mixture of frequency pattern composed of slow, fast and normal waves in short units of time (a second or less); poor amplitude pattern characterized by waves of very different heights in short units of time (less than a second); a noticeable amount of middle to high voltage positive discharges, spikey waves or dicrotic waves; or quick or moderate hyperventilation effect. The abnormal electroencephalograms are considered to have several of the following features:—a dominant frequency characteristic of waves slower than 8½ per second; more than 10 per cent single slow waves; more than 10 per cent serial slow waves less than 8½ per second; occasional high voltage bursts of the slow waves; a dominant frequency composed of very sharp 14 to 30 per second waves and amplitude running from 20 to 60 microvolts; bursts of these waves; a poor mixed frequency grouping; an irregular mixed amplitude grouping more pronounced than mentioned in the last category; a large number of diphasic spikes, or high voltage positive discharges, or cone-shaped waves of the positive sign; quick and prolonged hyperventilation effect; larval or continuous, high voltage saw-toothed, jagged, or flat-top waves; spike-and-wave patterns of high voltage; or high voltage paroxysmal bursts; quick and marked hyperventilation effect within a two minute hyperventilation period (60 inspirations and expirations). In the evaluation of the electroencephalogram more importance is attached to the frequency of the waves per second and the wave forms than to frequency grouping, amplitude and baseline stability. Certain patterns (saw-toothed, spike-and-wave patterns, etc.) like those mentioned in the last part of the previous sentence have the highest weight, even though they are less in incidence. Analysis of over three thousand electroencephalograms, clinical or otherwise, affords the basis for various items under the classification of normal, borderline and abnormal.[13]

I have further subdivided the abnormal records into a profoundly abnormal, a mildly abnormal and a focally abnormal type. No record was included in one of the abnormal groups unless it was unquestionably

13. Bagchi, B. K.; Howell, R. W., and Schmale, H. T.: The Electroencephalographic and Clinical Effects of Electrically Induced Convulsions in the Treatment of Mental Disorders, Am. J. Psychiat. **102**:49, 1945.

abnormal, but it is felt that the strikingly abnormal should be differentiated from records that show the ordinary amount of abnormality. The records with localizable focal changes are grouped separately because they reflect the pathoanatomic changes occurring in the disease.

ANALYSIS OF RESULTS

Of the 34 cases in this series, definitely abnormal electroencephalograms occurred in approximately 62.2 per cent, whereas borderline or normal electroencephalograms were present in 38 per cent. The exact figures are presented in table 2.

TABLE 2.—*Analysis of Electroencephalograms in 34 Cases of Multiple Selerosis*

Electroencephalographic Pattern	No. of Cases	Per Cent
Profoundly abnormal	4	11.8
Profoundly abnormal with focal signs	11	32.4
Mildly abnormal	6	17.6
Borderline	8	23.5
Normal	5	14.7

One notes that of the abnormal group fully 52.4 per cent revealed localizable focal abnormalities in the electroencephalogram. Of the 13 records that were normal or borderline, 62.0 per cent were borderline and 38.0 per cent were clearly normal. In only 5 instances (14.7 per cent) was a first zone colloidal gold curve observed. Four of these were in the group with abnormal electroencephalograms and 1 in the group of borderline activity.

The electroencephalogram was repeated after an interval of several months in 2 cases, with practically no change in the tracings. In these 2 instances the disease was still in exacerbation, but the clinical signs had shifted somewhat.

In a case in which the pneumonencephalogram revealed evidence of cortical atrophy in the left motor area, the electroencephalogram showed a lesion in the left anterior quadrant of the brain. The electrical signs in this case consisted of sawtooth top, spike, and spike and wave formations of 2, 3 and 4 per second frequencies and high voltage; these waves were diffusely scattered but were pronounced in the left anterior quadrant (fig. 1). The slow waves were seen in any ten to twenty second run. In this case the colloidal gold curve one day before the electroencephalographic recording was 0011100000 and the colloidal mastic curve 100000. The patient, a white woman aged 36, had a five year history of illness punctuated by two remissions. The electroencephalogram was made one day before the pneumoencephalogram. On the date of electroencephalographic recording, she exhibited euphoria, impaired memory, primary optic nerve atrophy (right eye),

nystagmus, 4 plus deep reflexes, loss of abdominal reflexes and 4 plus pathologic toe signs.

Analysis of the correlation of selected clinical signs and symptoms (not exclusive of each other) with the electroencephalographic abnormality is presented in table 3. One notes that the highest correlation in the abnormal group exists in the subgroup with associated focal signs, while in the "normal" group the percentage is probably significantly higher in the subgroup of borderline activity. One notes also that the highest correlation in all the subgroups is that in the one with focal signs. In table 4 the totals for the groups are presented. This table demonstrates the statistical significance of the correlations even more clearly than does table 3.

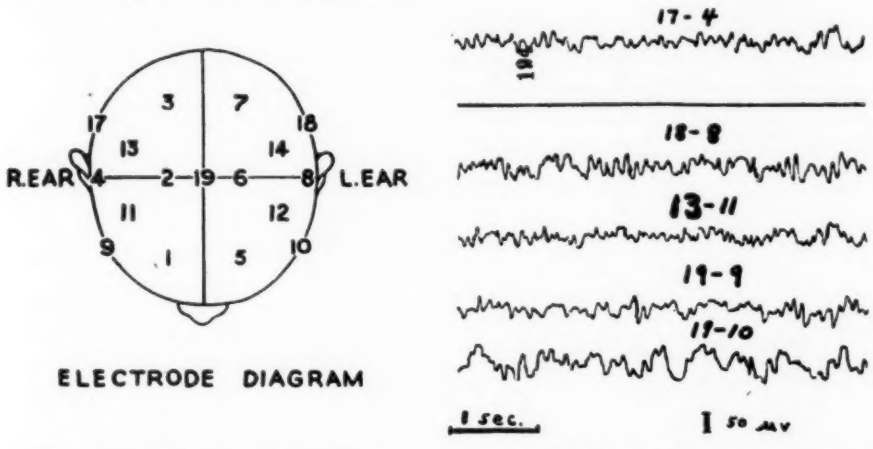

Fig. 1.—Electroencephalogram in a case of multiple sclerosis with cortical atrophy in the left anterior quadrant of the brain.

TABLE 3.—*Comparison of Selected Clinical Manifestations and Electroencephalographic Findings in 34 Patients*

Manifestation	Total No. of Cases	Profoundly Abnormal		Profoundly Abnormal with Focal Signs		Mildly Abnormal		Borderline		Normal	
		No.	%	No.	%	No.	%	No.	%	No.	%
Mental changes	26	2	7.7	11	42.3	2	7.7	8	30.7	3	11.5
Sphincter disturbances	23	1	4.3	9	39.1	4	17.4	7	30.4	2	8.7
Pathologic toe signs	33	2	6.1	12	36.3	6	18.2	8	24.2	5	15.1
Pathologic deep reflexes	31	3	9.7	12	38.7	4	12.9	8	25.8	4	12.9
Cerebellar signs	31	3	9.7	11	35.5	6	19.4	6	19.4	5	16.1
Nystagmus	30	3	10.0	11	36.7	6	20.0	5	16.7	5	16.7
Diplopia	17	3	17.6	4	23.5	4	23.5	3	17.6	3	17.6
Central scotoma	11	1	9.1	3	27.3	2	18.2	3	27.3	2	18.2

COMMENT

Although the attempt was made in this study to exclude as many complicating factors as possible, some are admittedly difficult to eliminate. In an effort to control the effect of hyperventilation on the

record, forced breathing was limited to two minutes. This is in accordance with the experience of many workers (Gibbs, Davis and Lennox [14]; Davis and Wallace [15]; Gibbs, Gibbs and Lennox [16]; Brazier, Finesinger and Schwab,[17] and Bagchi [18]), all of whom found that pronounced abnormalities appeared after the second minute of hyperventilation, even in normal adults.

Despite the fact that Hoefer and Guttman [5] had their patients overventilate for five minutes, their percentage of abnormal tracings was only 44.0 per cent, as compared with 62.0 per cent in the present study. I am unable to explain this difference except on the basis that in approximately 10 per cent of their cases the disease was in remission when the electroencephalograms were made, while in all the cases in the present series it was in exacerbation. It is also possible that by the time I have accumulated another 60 or 70 cases my percentage of abnormalities may be reduced to that which these authors obtained.

TABLE 4.—*Correlations of Electroencephalographic Findings and Clinical Manifestations for All Groups*

	Totals for "Abnormal" Group		Totals for "Borderline-Normal" Group	
	Number	Per Cent	Number	Per Cent
Mental changes	15	57.7	11	42.3
Sphincter disturbances	14	60.9	9	39.1
Pathologic toe signs	20	60.6	13	39.4
Pathologic deep reflexes	19	61.3	12	38.7
Cerebellar signs	20	64.5	11	35.5
Nystagmus	20	66.7	10	33.3
Diplopia	11	64.7	6	35.3
Central scotoma	6	54.5	5	45.5

My results do not agree with those obtained by other authors (Berger,[6] Lemere,[7] Gibbs and Gibbs,[8] Freeman,[9] Freeman and Cohn [10]) in that they noted only insignificant electroencephalographic changes. The claims of Freeman and Cohn [10] and Winkleman [12] that cortical lesions are not found in cases of multiple sclerosis and that one, there-

14. Gibbs, F. A.; Davis, H., and Lennox, W. G.: The Electroencephalogram in Epilepsy and in Conditions of Impaired Consciousness, Arch. Neurol. & Psychiat. **34**:1133 (Dec.) 1935.

15. Davis, H., and Wallace, W. M.: Factors Affecting Changes Produced in Electroencephalogram by Standardized Hyperventilation, Arch. Neurol. & Psychiat. **47**:606 (April) 1942.

16. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. C.: Electroencephalographic Response to Overventilation and Its Relation to Age, J. Pediat. **23**:497, 1943.

17. Brazier, M. A. B.; Finesinger, J. E., and Schwab, R. S.: Characteristics of the Normal Electroencephalogram: III. The Effect of Varying Blood Sugar Levels on the Occipital Cortical Potentials in Adults During Hyperventilation, J. Clin. Investigation **23**:319, 1944.

18. Bagchi, B. K.: Personal communication to the author.

fore, must not expect electroencephalographic abnormalities are subject to challenge on a number of counts. Wilson,[2] Hassin,[19] Freeman [20] and Lowenberg,[21] among others, have all demonstrated cortical lesions in cases of multiple sclerosis. I personally have studied Nissl sections in 3 cases of multiple sclerosis in Lowenberg's collection, all of which revealed unmistakable lesions in the cortex. Such a section is reproduced here (fig. 2). I am not prepared to state the incidence of such cortical lesions, as the 3 cases referred to here were selected at random from the study collection in the laboratory of neuropathology of the

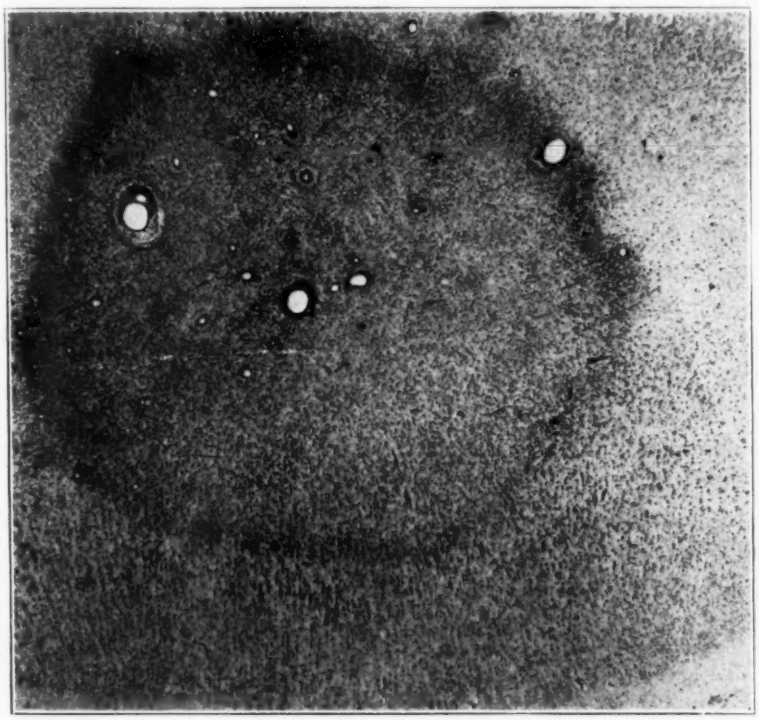

Fig. 2.—Section of the cortex in a case of multiple sclerosis; Nissl stain.

Neuropsychiatric Institute of the University of Michigan, but I hope to announce the results of such a study at a later date. Such lesions have also been observed [21] in the region of the hypothalamus. That islands of demyelination occur in the white matter of the brain is conceded by all. Furthermore, it is entirely possible for degeneration of cortical neurons to occur by virtue of retrograde wallerian degeneration

19. Hassin, G. B.: Histopathology of the Peripheral and Central Nervous System, New York, Paul B. Hoeber, Inc., 1933.

20. Freeman, W.: Neuropathology, Philadelphia, W. B. Saunders Company, 1933.

21. Lowenberg, K.: Personal communication to the author.

in instances in which destruction of afferent axons has occurred as a result of demyelination. It follows, then, that electroencephalographic abnormality may result from lesions in the cortex or the white matter, the thalamus or the hypothalamus. A lesion in the fiber tracts that connect the hypothalamus with the dorsomedial nucleus of the thalamus, or that nucleus with the cortex, is just as capable of producing aberrations in the brain waves as is a lesion of the gray substance itself. Murphy and Gellhorn,[22] using the strychnine spike technic, found strong evidence for the hypothalamic origin of the alpha rhythm and the relay of these action potentials in the dorsomedial nucleus of the thalamus on their way to the cortex.

In connection with the close physiologic relation between the hypothalamus and the cortex, one may well consider the implications of involvement of the hypothalamus or of the hypothalamic tract in the emotional disorganization of patients with multiple sclerosis. Ranson,[23] Cannon [24] and Bard [25] represented the hypothalamus as the center for correlation of emotional expression. The association between this structure and the course of the disease, though not yet demonstrated, may have some bearing on the opinion entertained by experienced observers (Camp,[4] Mohr,[26] Jelliffe [27]) that multiple sclerosis is a psychosomatic disorder.

In this study, I have found surprisingly little correlation between the colloidal gold curve and the electroencephalogram. Although 62 per cent of the patients had abnormal electroencephalograms, only 14.7 per cent had first zone colloidal gold curves. These findings are significant not only because of the apparently greater sensitivity of the electroencephalogram, but also because of the low incidence of first

22. Murphy, J. P., and Gellhorn, E.: The Influence of Hypothalamic Stimulation on Cortically Induced Movements and on Action Potentials of the Cortex, J. Neurophysiol. **8**:341, 1945. Further Investigations on Diencephalic Cortical Relations and Their Significance for the Problem of Emotion, ibid. **8**:431, 1945; Hypothalamic Facilitation of the Motor Cortex, Proc. Soc. Exper. Biol. & Med. **58**:114, 1945.

23. Ranson, S. W.: The Hypothalamus: Its Significance for Visceral Innervation and Emotional Expression, Tr. Coll. Physicians, Philadelphia **2**:222, 1934.

24. Cannon, W. B.: Again the James-Lange and the Thalamic Theories of Emotion, Psychol. Rev. **38**:281, 1931.

25. Bard, P.: A Diencephalic Mechanism for the Expression of Rage with Special Reference to the Sympathetic Nervous System, Am. J. Physiol. **84**:490, 1928.

26. Mohr, F.: Psychophysische Behandlungsmethoden, Leipzig, S. Hirzel, 1925.

27. Jelliffe, S. E.: Multiple Sclerosis and Psychoanalysis: A Preliminary Statement of a Tentative Research, Am. J. M. Sc. **161**:666, 1921.

zone gold curves, as compared with the 25 per cent incidence in the series of Merritt and Fremont-Smith.[28]

I am unable to explain why localizable electroencephalographic foci were not always compatible with the clinical picture, except to point to the relative grossness of the clinical examination as compared with the delicacy of electrocortical measurements. Despite the fact that clinical neurologic diagnosis is so much more accurate than that of many other branches of medicine, it may require a relatively gross lesion to produce recognizable signs.

I was unable to find a specific electroencephalographic pattern in cases of multiple sclerosis, the abnormal tracings revealing a range from extremely slow waves (1 to 2 per second) to high frequency activity, from spike and dome to diphasic spikes to sawtooth top formations and from medium to high to extremely high voltage. Some of the records were indistinguishable from those seen in cases of ordinary idiopathic convulsive disorders, whereas a few resembled, but were not entirely similar to, those associated with neoplastic lesions.

CONCLUSIONS

The electroencephalogram was abnormal in 62 per cent of 34 cases of multiple sclerosis in exacerbation.

In this series an abnormal electroencephalogram was more consistently associated with multiple sclerosis in exacerbation than was a first zone colloidal gold curve.

This series revealed no electroencephalographic signs specifically diagnostic of multiple sclerosis.

In obscure cases with no objective evidence of cortical or subcortical involvement, the electroencephalogram may be used to differentiate multiple sclerosis from pure spinal cord disease.

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28. Merritt, H. H., and Fremont-Smith, F.: The Cerebrospinal Fluid, Philadelphia, W. B. Saunders Company, 1938.

GANGRENE OF FACE FOLLOWING OCCLUSION OF POSTERIOR INFERIOR CEREBELLAR ARTERY

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CHANGES in the skin as a result of disease of the trigeminal nerve have rarely been reported. Most such lesions followed surgical section of this nerve or injections in its peripheral pathway for the relief of tic douloureux. Karnosh and Scherb [1] reported an eczematous eruption in the distribution of the first and second divisions following section of these branches. Harris [2] stated that superficial ulcerations at the ala nasi, and more rarely on the cheek and forehead, follow injections of alcohol into the gasserian ganglion in a small percentage of cases. Schornstein [3] reported 8 cases of progressive ulceration, commencing at the ala nasi, subsequent to retroganglionic section and injection of alcohol into the ganglion. Necrosis of the maxillary mucous membrane occurring twelve years after a retrogasserian neurectomy was recorded by Dechaume and Delibéros.[4] They stated that an ill fitting denture was the probable precipitating cause. Three cases of postoperative erosion of the nasal region were observed by Peet [5] in 1,000 resections of the sensory root. Mixter [6] stated that after section of the posterior root paraesthesias may be so distressing that "one will often find a patient with a bit of the skin . . . scratched off." Becker [7] reported an erythemato-

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1. Karnosh, L. J., and Scherb, R. F.: Trophic Lesions in Distribution of the Trigeminal Nerve, J. A. M. A. **115**:2145 (Dec. 21) 1940.

2. Harris, W.: Tic Douloureux, Brain **63**:209, 1940.

3. Schornstein, J.: Erosion of the Alae Nasi Following Fifth Nerve Denervation, J. Neurol. & Psychiat. **6**:46, 1943.

4. Dechaume and Delibéros: Ulcération trophique au maxillaire supérieur chez un opérée de neurotome rétrogassérienne totale, Rev. de stomatol. **38**:194, 1936.

5. Peet, M.: Post-Herpetic Neuralgia, J. A. M. A. **92**:1502 (May 4) 1933.

6. Mixter, W. J., in discussion on Grant, F. C.; Groff, R. A., and Lewy, F. H.: Section of the Descending Spinal Root of the Fifth Cranial Nerve, Arch. Neurol. & Psychiat. **43**:498 (March) 1940.

7. Becker, S. W.: Dermatitis in Association with Disease or Injury of the Peripheral Nerves, Arch. Dermat. & Syph. **12**:235 (Aug.) 1925.

vesicular eruption on the side of resection of a fifth nerve root. Netherton [8] saw a reddish area develop on the forehead, temple, lid, cheek and angle of the mouth after section of the sensory root and avulsion of the first and second divisions of the nerve.

Similar, but rarer, cutaneous changes are associated with other lesions of the pathway of the fifth cranial nerve. In a case of acoustic neuroma reported by Schornstein,[3] in which there were palsy and anesthesia of the left side of the face, ulceration developed at the ala nasi, with progressive recession of this structure. We found only 2 reports of trophic changes with intramedullary involvement of the fifth nerve. Karnosh and Scherb [1] noted a case of syringobulbia in which a cicatrizing ulcer formed on the involved side of the face, as well as a case of occlusion of the posterior inferior cerebellar artery with multiple ulcers on the analgesic side. A review of 81 cases of occlusion of the posterior inferior cerebellar artery from the literature and of 14 private cases revealed no other instance of severe alterations in the skin. Patches of nasal herpes (Ramsbottom and Stopford,[9] Hall [10]) and erosion of the skin in the region of the ala nasi (Wallenberg [11]) have been recorded.

Trauma to the involved area of the face is often a significant factor in accounting for the appearance of these trophic changes. Schornstein [3] and Mixter [6] emphasized the distressing paresthesias and the consequent self-inflicted trauma in such cases. Dechaume and Delibéros [4] stated that an ill fitting denture was the traumatic factor. In our case the constant pressure of a Levin tube was a precipitating factor.

REPORT OF A CASE

On Sept. 22, 1945, a white man aged 53, married, was admitted to the Morrisania City Hospital for the second time. Two weeks previously he had entered the hospital for acute failure of the left side of the heart. His condition improved and he left, against advice, in three days. For a few days before the second admission he had been weak and had complained of dizziness. On admission he looked weak, with evident dyspnea. The temperature was 99.2 F.; the pulse rate was 108 and the respiratory rate 24, per minute. The blood pressure was 195 systolic and 110 diastolic. The heart sounds were rapid and of poor quality. There were rales at the bases of both lungs.

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8. Netherton, E. W.: Persistent Dermatitis: An Unusual Sequel of Radical Operation for Fifth Nerve Neuralgia, J. A. M. A. **100**:722 (March 11) 1933.

9. Ramsbottom, A., and Stopford, J. S. B.: Occlusion of the Posterior Inferior Cerebellar Artery, Brit. M. J. **1**:364, 1924.

10. Hall, G.: A Case of Occlusion of the Posterior Inferior Cerebellar Artery, Arch. Neurol. & Psychiat. **3**:584 (May) 1920.

11. Wallenberg, A.: Klinische Beiträge zur Diagnostik akutes Herderkrankungen der verlängerten Mark und der Brücke, Deutsche Ztschr. f. Nervenh. **19**:227, 1901.

The diagnosis on his admission was hypertensive vascular disease with enlarged heart and mild congestive heart failure. The patient was placed under a dehydration regimen with rest in bed. On the day after his admission it was noted that he had difficulty in swallowing. Neurologic examination showed absence of sweating on the left side of the face; the pupil and palpebral fissure on the left side were smaller than those on the right; the pupils were round and regular and reacted to light and in accommodation. There was lateral nystagmus on gaze to the left. The fundi showed retinal arteriosclerosis. There were hypalgesia on the left side of the face and areflexia of the left cornea; touch sensibility was spared; hypalgesia and hypothermesthesia were noted on the right side of the body. There were left palatoplegia and difficulty in swallowing. The voice was hoarse, and the patient recognized a recent change in its timbre. There was cerebeller incoordination of the left extremities. The deep reflexes were active and equal on the two sides. On the basis of these findings, a diagnosis of occlusion of the left posterior inferior cerebellar artery was made. The Babinski sign, elicited bilaterally, was attributed

Gangrene of the face following occlusion of the posterior inferior cerebellar artery.

to other vascular lesions. In view of the severe difficulty in swallowing, a Levin nasal tube was inserted in the left side to facilitate feeding.

On October 12, redness and swelling were noted about the left ala nasi. The tube was removed and sulfadiazine administered. The swelling and redness gradually disappeared, and on November 1 an ulceration of the ala was noted. There was no sugar or albumin in the urine. The blood count showed 11,200 white cells, with 72 per cent polymorphonuclear leukocytes and 28 per cent lymphocytes. The urea nitrogen was 21 mg. per hundred cubic centimeters. The Wassermann reaction of the blood was negative. There was progressive ulceration of the ala of the nostril. The patient was discharged on December 15.

The patient was readmitted on Feb. 7, 1946 because of the progressive ulceration of the nostril. The condition had developed to the point where half the nostril and some of the adjacent area of the cheek were involved in the process. The lesion was painless. The Kahn reaction of the blood was negative. A dermatologic consultant reported the lesion to be nonsyphilitic. A biopsy, performed on February 18, revealed no evidence of syphilitic inflammatory process or of a neoplasm. The patient was discharged without improvement.

CONCLUSION

A case of occlusion of the posterior inferior cerebellar artery with severe trophic changes in the face is reported.

The rarity of such trophic changes after occlusion of the posterior inferior cerebellar artery is emphasized.

Trauma to the face is a significant etiologic factor. The pressure of a nasal tube inserted in the affected side was considered the traumatic factor in this case.

Nasal tubes should be inserted on the uninvolved side in cases of unilateral sensory impairment of the face.

1882 Grand Concourse.

UNTOWARD REACTIONS TO CURARE CONSEQUENT TO VAGAL HYPERACTIVITY FOLLOWING ELECTROSHOCK CONVULSIONS

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AT TIMES it is necessary to diminish the violence of convulsions induced in the treatment of mental diseases; this has led in some instances to the practice of premedication with curare, in the form of "intocostrin." While this procedure has been employed successfully many times, its use creates certain hazards not ordinarily associated with convulsant therapy. The commonly recognized untoward manifestation associated with curarization is respiratory paralysis. This appears to be of two types, consequent either (*a*) to severe generalized muscular weakness, which may be overcome rapidly with neostigmine methylsulfate, or (*b*) to central depression of respiration, as noted by Fegler.[1] The latter type may be associated with no unusual weakness of skeletal muscle[2] and is not noticeably benefited by neostigmine.[3] These reactions, though hazardous, are amenable to rational therapy and become dangerous largely through lack of preparedness for their occurrence. Still another type of accident has, however, received only scattered notice; it consists in respiratory difficulty associated with wheezing, and often combined with

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1. Fegler, J.: The Action of Curare on the Respiratory Center, J. Physiol. **100**:417, 1942.

2. Cummins, J. A.: Metrazol Complications as Affected by the Use of Curare, Canad. M. A. J. **47**:326, 1942.

3. Woolley, L. F.; Jarvis, J. R., and Ingalls, G. S.: On the Use of Curare in Modifying Convulsive Shock, J. Nerv. & Ment. Dis. **96**:680, 1942. Smith, L. H.; Hastings, D. W., and Hughes, J.: Immediate and Follow-Up Results of Electroshock Therapy, Am. J. Psychiat. **110**:351, 1943. Cummins, J. A.: Atypical Post-Metrazol Status Epilepticus, ibid. **101**:117, 1944.

marked bradycardia and cardiac arrhythmia.[4] Two such instances, 1 of them fatal, have recently been observed here. It was decided, therefore, to call attention to this type of reaction by presenting the observations in these cases; certain theoretic considerations bearing on the nature of the disorder and on its treatment will also be discussed.

REPORT OF CASES

CASE 1.—A broker, aged 40, entered the hospital on June 18, 1946, complaining of feeling greatly depressed. The family history revealed that the patient's father died of disease of the coronary arteries and hypertension. The patient's mother was described as a selfish, unstable and domineering woman who in recent years had become psychotic. The marital and past personal histories were not remarkable. The first evidence of mental illness appeared when the patient was 24 years of age, at which time palpitation and a feeling of depression were noted. These wore off over a period of months and did not recur until ten years later, when unfavorable war news upset the patient. Again, these complaints regressed; but six years later, i. e., nine months before his admission, business difficulties and trouble with his deluded mother caused the patient a good deal of distress. Palpitation, dyspepsia, flatulence, insomnia, weakness and a feeling of tightness in the head become troublesome, and an initial feeling of unhappiness soon became a deep depression. The patient entered another hospital, where psychotherapy was instituted, without, however, any improvement in this condition; this experience aroused so much resentment in the patient against the staff that he left. On his admission to this hospital two months later, he was depressed, retarded and preoccupied with his somatic complaints. Physical examination revealed nothing of significance except for a coarse tremor and a blood pressure of 140 systolic and 90 diastolic. The urine was normal except for an occasional leukocyte in centrifuged specimens. The hemoglobin was 14.0 Gm. per hundred cubic centimeters; the erythrocyte count was 5,600,000, and the leukocyte count, 8,500. The fasting blood sugar concentration was 76 mg. and the nonprotein nitrogen 32 mg., per hundred cubic centimeters. The Hinton test of the blood gave a negative reaction. A week after admission he was given an electric shock treatment. The next day pain in the chest and back troubled the patient; roentgenographic studies revealed several compression fractures of the spine and an area of density in the lung, consistent with either atelectasis or infarction. A second treatment was given seven days later, "intocostrin" being used at this time. The patient was given 72 units intravenously, i. e., 0.42 unit per pound (0.9 unit per kilogram) of body weight, in one and one-half minutes. The pulse rate was 80 and the respiratory rate 16 per minute, and the blood pressure was 135 systolic and 90 diastolic. Muscular strength was not notably impaired by this dose of "intocostrin," but electric shock nevertheless was administered. The patient had a vigorous convulsion lasting forty-two seconds, followed by a period of apnea lasting five seconds.

4. (*a*) Bellet, S.; Kershbaum, A., and Furst, W.: The Electrocardiogram During Electric Shock Treatment of Mental Disorders, Am. J. M. Sc. **201**:167, 1941. (*b*) Jones, G. L., and Pleasants, E. N.: Curare Modification of Therapeutic Convulsions, Dis. Nerv. System **4**:17, 1943. (*c*) Woolley, L. F.: Immediate Circulatory and Respiratory Effects of Convulsive Shock: Curare-Protected Metrazol and Electric Shock, J. Nerv. & Ment. Dis. **100**:1, 1944.

When respiration returned, it was labored and wheezing, and the rate was 6 per minute. The patient was deeply cyanotic, as well as limp and pulseless. Thirty seconds later the pulse rate was 40 and after another minute it rose to 88 a minute. At this time the blood pressure was 200 systolic and 110 diastolic. The patient thrashed about violently for brief periods from time to time. The respiratory rate was still 6 per minute and remained wheezing and severely labored for several minutes. Artificial respiration was employed, and neostigmine methylsulfate and a mixture of 95 per cent oxygen and 5 per cent carbon dioxide were administered. Electrocardiograms were made during this entire period; they showed complete asystole, lasting seventeen seconds, immediately after the convulsion. When the heart beat returned, a variety of arrhythmias, including idio-

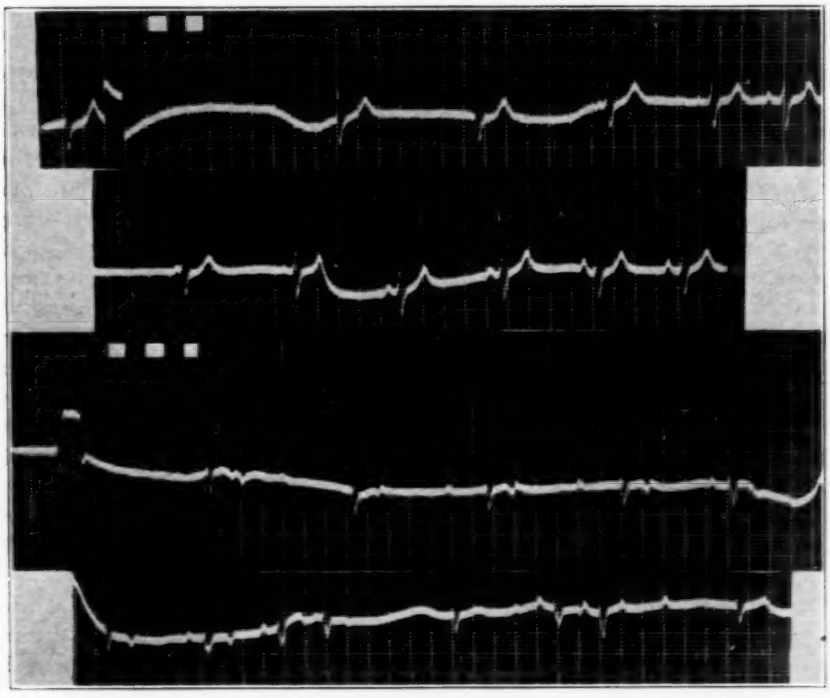

Fig. 1 (case 1).—Electrocardiogram on resumption of the heart beat after a period of asystole.

ventricular rhythm, nodal beats and heart block, were present, but these wore off in the next minute (fig. 1). The pulse and respiration were both normal five minutes after the convulsion. The next day, in order to determine whether the patient had an abnormally active vagus nerve, the sensitivity of the carotid sinus was tested. No hypersensitivity was found. A week later another convulsion was induced, this time without "intocostrin." Before the convulsion the pulse rate was 108, the respiratory rate 20 and the blood pressure 150 systolic and 90 diastolic. The convulsion lasted forty-five seconds and was followed by a period of apnea of eight seconds. After the convulsion the pulse rate was 72, the respiratory rate 14 and the blood pressure 150 systolic and 80 diastolic. No respiratory difficulty occurred after the convulsion, and the only change seen in the electrocardiogram was pronounced sinus arrhythmia. The vigor of the muscular con-

tractions of the convulsion, as measured by the rise in venous pressure which occurred,[5] was only slightly greater than that which had occurred when "intocostrin" was given (fig. 2).

Case 2.—B. M., a housewife aged 70, first entered the hospital on May 3, 1942, having been depressed for six months. The family history revealed that the patient's father died at the age of 75 of prostatism and arteriosclerosis; he had been psychotic terminally. The patient's mother died at the age of 87, with senile psychosis. One brother had a depression at the age of 62 and the other died of cancer of the stomach. The family otherwise was not remarkable except for its

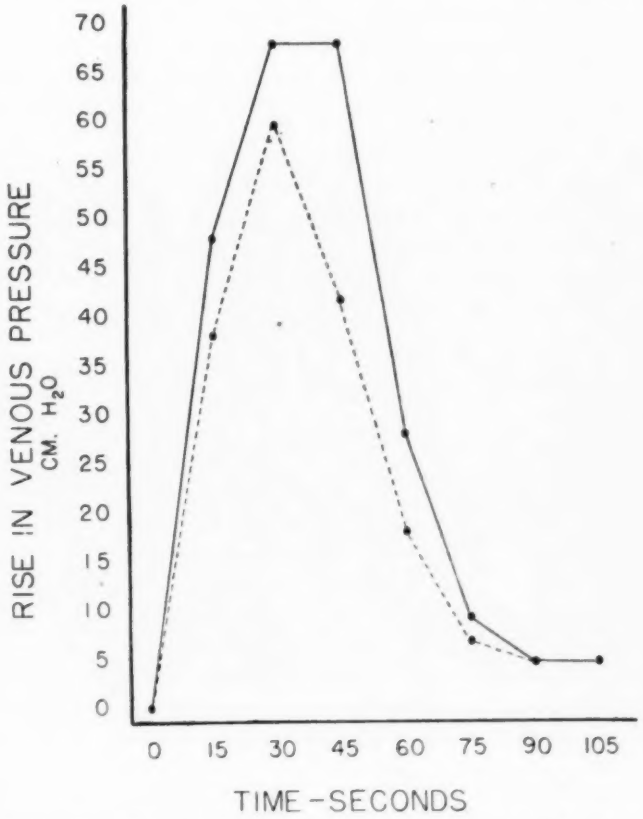

Fig. 2 (case 1).—Changes in venous pressure during electrically induced convulsions. The values without "intocostrin" are shown by the solid line; the values with "intocostrin" by the line of dashes.

strong religious principles. The past history was not significant until six years before her admission, when the patient fell on her head and was unconscious for several hours. The marital history was not contributory except that no children were desired. The present illness began with the patient's becoming quiet and detached after the death of her brother, of carcinoma; she had been very fond of him. She expressed worry concerning her own stomach and was studied by a

5. Altschule, M. D.; Sulzbach, W. M., and Tillotson, K. J.: Effect of Electrically Induced Convulsions on Peripheral Venous Pressure in Man, Arch. Neurol. & Psychiat. **58**:193 (Aug.) 1947.

physician, who detected disease of the gallbladder. He prescribed vitamins and gave reassurance. She felt better for a time but soon became more detached and depressed; she made an attempt at suicide shortly before admission.

On examination, the patient appeared retarded, perplexed, agitated and seclusive. There was evidence of generalized arteriosclerosis. The blood pressure ranged from 160 systolic and 90 diastolic to 180 systolic and 120 diastolic. The heart was normal except for an accentuated ringing second aortic sound. The tongue was slightly smooth, and the fingers presented Heberden's nodes. The specific gravity of the urine ranged from 1.011 to 1.021. Examination of the urine revealed nothing abnormal. The erythrocyte count was 5,200,000, with a hemoglobin content of 15.4 Gm. per hundred cubic centimeters. The leukocyte count was 6,300. The fasting blood sugar was 86 mg. and the nonprotein nitrogen 25 mg., per hundred cubic centimeters. The Hinton reaction of the blood was negative. The electrocardiogram showed normal rhythm, a rate of 100, a prominent Q wave in lead III, a deep S wave and low T wave in lead I, an inverted T wave in lead IV and a diphasic P wave in lead III. The patient was in the hospital from May 3, 1942 to Jan. 27, 1943. She was given two courses of electric shock therapy, consisting of seven and eight treatments, respectively; the first was given in October and the second in December 1942. Improvement occurred after each treatment but was not long maintained. Electrocardiograms after shock showed some increase in the height of the T wave in lead I, and the T wave in lead IV became upright. The patient was discharged as somewhat improved after eight months and twenty-four days of hospitalization.

After discharge, the patient gradually became anoretic, depressed and retarded to the point of muteness. She was readmitted on April 11, 1943. Her physical condition was unchanged. Laboratory tests, including examinations of the blood and urine, electrocardiographic study and blood chemical analysis, gave results similar to those on the previous admission. In addition, lumbar puncture revealed normal pressure and dynamics and normal constituents of the spinal fluid. The patient's condition was unchanged until November 1943, when she was given five electric shock treatments. She became more responsive, and at times was either irritable or facetious. However, she soon relapsed to her former mutism. In December 1944 a course of eight shock treatments had the same effect. During this period she gradually became more untidy. In April 1945 an unexplained vaginal discharge developed. On Nov. 28, 1945 prefrontal lobotomy was performed. The patient became somewhat more cooperative, but her condition was otherwise not improved. Electric shock was again given on May 27, 1946. The electrocardiogram ten minutes before the shock was the same as that previously noted; the pulse rate was 104 and the respiratory rate was 20 per minute, and the blood pressure 204 systolic and 118 diastolic. Three cubic centimeters of "intocostrin," i. e., 0.44 unit per pound (0.98 unit per kilogram) of body weight, was given intravenously over a period of two minutes by the clock. The electrocardiogram a few minutes later was unchanged. The patient was not greatly weakened by curare and resisted placement of the mouth gag. An electric shock was given, resulting in a moderate convulsion. Immediately after the end of the convulsion the electrocardiogram was found to be unchanged except for a pulse rate of 60. The respiration and blood pressure were unchanged. A few minutes later she became pulseless and ceased to breathe except in infrequent, noisy gasps. Oxygen given intratracheally resulted in a return of normal cardiac action for a short time, with a pulse rate of 30 to 40 per minute. The patient, however, did not recover, in spite of the administration of stimulant drugs.

Autopsy was performed four hours post mortem. The brain and meninges were everywhere adherent. A large amount of spinal fluid ran off when the meninges were cut. Old lobotomy scars were noted; these will be described elsewhere. The heart weighed 420 Gm. and appeared normal in size and shape. Epicardial fat was abundant. The pulmonary artery contained partly clotted blood. The coronary arteries were soft. Injection and dissection of the coronary arteries [6] showed a few atheromatous plaques but no occlusions or collateral circulation (fig. 3). The endocardium, valves and myocardium were normal in color and showed no scarring. The lungs did not feel heavy. Their surfaces were a mottled pinkish gray except for both lower lobes and for the posterior portions of the upper lobes, which were a dark purplish red. No adhesions were noted. The apex of the right lung bore a puckered, fibrosed area 1 cm. in diameter. Both lower lobes and the posterior portions of the upper lobes felt rubbery; the rest of the lungs was soft and fluffy. No areas of consolidation were seen. The bronchi

Fig. 3 (case 2).—Roentgenogram of the injected heart.

contained a moderately increased amount of pinkish white mucoid secretion. The mucosae appeared slightly congested. The pulmonary arteries contained atheromatous plaques a few millimeters in diameter, scattered about so that approximately a quarter of the intima was arteriosclerotic. No thrombi were noted. Section revealed that the lungs were dry and crepitant in the anterior portions of the upper lobes, but elsewhere were congested and less well aerated than normal. No signs of infection were seen. The other gross changes consisted in congestion of the viscera; a multitude of fine abdominal adhesions; a slightly thickened gallbladder, containing a stone several centimeters in diameter; many scattered mural hemorrhages, 1 to 3 cm. in diameter, in the small intestine; a few shallow, irregular pits on the surfaces of the kidneys; a nodule 1 cm. in diameter on the surface of the liver; a large pancreas; several tiny fibroid tumors in the uterus; a smooth

6. Schlesinger, M. J.: An Injection Plus Dissection Study of Coronary Artery Occlusions and Anastomoses, Am. Heart J. **15**:528, 1938.

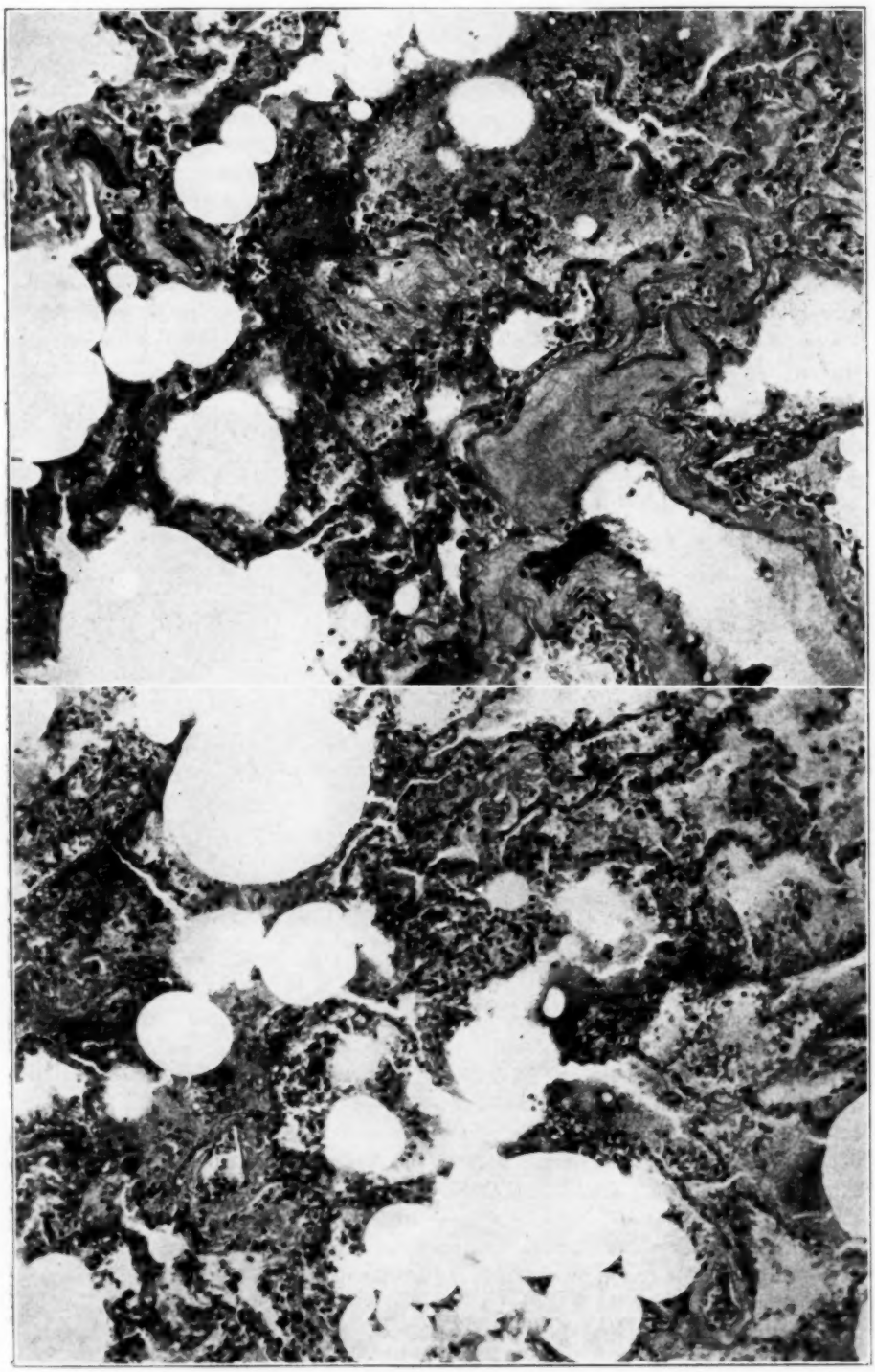

Fig. 4 (case 2).—Early hemorrhagic pulmonary edema.

endometrial polyp, 2 cm. in diameter, and slight to moderate atheromatous formation in the aorta.

Microscopic examination confirmed the gross observations and revealed, in addition, early hemorrhagic pulmonary edema (fig. 4); a few tiny fibrosed areas in the heart; slight fatty infiltration of the pancreas, liver and heart; a markedly fibrosed hemangioma on the surface of the liver; acute degenerative changes in the adrenal cortex; hyalinization of the arterioles of the spleen and pancreas, and scattered small clusters of completely fibrosed glomeruli, together with foci of scarring and chronic inflammatory cell infiltration in the kidneys.

The final diagnoses were cerebral edema, atelectasis, pulmonary edema and generalized and renal arteriosclerosis.

COMMENT

In both cases described here, evidence of the action of strong vagal influences was present during the untoward reaction to "intocostrin"; this evidence consisted in bradycardia or asystole, cardiac arrhythmia and wheezing respiration. In addition, the occurrence of pulmonary edema might be construed as evidence of vagal hyperactivity.[7]

"Intocostrin" alone in the doses used has no effect on the electrocardiogram[8]; electroshock therapy alone does not give rise to the musical wheezing of bronchospasm, and its effects on the heart indicate only a slight or moderate degree of stimulation of the cardiac branch of the vagus nerve.[10] It is apparent, however, that the two together result in strong vagal effects. Studies on the pharmacologic action of curare and its constituent alkaloids afford suggestive evidence bearing on this matter.

Curare is a variable mixture of alkaloids which paralyze skeletal muscle, together with a number of other substances, known and unknown, which exhibit a greater or less degree of pharmacologic activity. The material in "intocostrin" which has the property of paralyzing skeletal muscle consists largely or entirely of the alkaloid *d*-tubocurarine, a quaternary base; the associated impurities are largely tertiary

7. Luisada, A.: The Pathogenesis of Paroxysmal Pulmonary Edema, Medicine **19**:475, 1940. Henneman, P. H.: Acute Pulmonary Edema with Special Reference to Experimental Studies, New England J. Med. **235**:59, 1946.

8. Altschule, Sulzbach and Tillotson.[10b] Ruskin, A.; Ervalt, J., and Decherd, G.: The Electrocardiogram of Curarized Human Subjects, Dis. Nerv. System **4**:335, 1943.

9. Footnote omitted.

10. (*a*) Bellet and others.[4a] (*b*) Altschule, M. D.; Sulzbach, W. M., and Tillotson, K. J.: Significance of Changes in the Electrocardiogram After Electrically Induced Convulsions in Man, Arch. Neurol. & Psychiat. **58**:716 (Dec.) 1947.

bases.[11] Harris and Harris[12] several years ago showed that "intocostrin" both in vitro and in vivo, strongly depresses the cholinesterases of the blood, i.e., the substances which tend to inhibit vagal action. The work of McIntyre and King[13] suggested that this effect might be related to the presence of impurities in "intocostrin,"[11b] for they detected no such activity in *d*-tubocurarine. More recently Harris and associates[14] confirmed this concept by demonstrating the anticholinesterase effects of tertiary bases found in "intocostrin"[11b]; however, these authors showed that *d*-tubocurarine possesses minor degrees of such activity also.

Evidences of cholinergic effects are seen during all seizures induced with electric shock. Indeed, passage of the electricity through the brain gives rise to such manifestations, i. e., flushing, hypotension, lacrimation and, at times, bradycardia, even in the absence of seizures. During seizures there are, in addition, salivation and cardiac arrhythmia.[10] Apparently, these vagal effects are prevented from becoming dangerous by an adrenergic discharge, manifested by late pallor, piloerection and hypertension, which occurs during the convulsion. Conceivably, anything which disturbed this balance might cause untoward reactions. It is felt that the anticholinesterase activity of impurities in "intocostrin,"[11b] fortified by the milder similar effects of *d*-tubocurarine, may upset this balance by exaggerating the vagal effects of electrically induced convulsions. Pertinent evidence relative to this concept is found in the work of Cleckley and associates.[15] These authors showed that if the sympathetic nervous system was largely paralyzed by spinal anesthesia as high as the first to the third thoracic segments before convulsant therapy, the balance between adrenergic

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11. (*a*) Wintersteiner, O., and Dutcher, J. D.: Curare Alkaloids from Chondodendren Tomentosum, Science **97**:467, 1943. (*b*) Since the observations of the present study were made, the composition of "intocostrin" has been changed, so that the tertiary bases are no longer present in the solution.

12. Harris, M. M., and Harris, R. S.: Effect in Vitro of Curare and Beta-Erythroidin Hydrochloride on Cholinesterase of Human Blood Serum: I., Proc. Soc. Exper. Biol. & Med. **46**:619, 1941; Effect in Man of Curare and Metrazol on Cholinesterase Activity of Blood Serum: II., ibid. **46**:623, 1941.

13. McIntyre, A. R., and King, R. E.: *d*-Tubocurarine Chloride and Cholinesterase, Science **97**:69, 1943.

14. Harris, M. M., and Harris, R. S.: Effect in Vitro of Curare Alkaloids and Crude Curare Preparations on True and Pseudo Cholinesterase, Proc. Soc. Exper. Biol. & Med. **56**:223, 1944.

15. Woodbury, R. A.; Hamilton, W. F.; Cleckley, H. M., and Volpitto, P. P.: The Effect of Metrazol upon the Blood Pressure of Man and Dog, J. Pharmacol. & Exper. Therap. **73**:431, 1941. Cleckley, H.; Hamilton, W. P.; Woodbury, R. A., and Volpitto, P. P.: Blood Pressure Studies in Patients Undergoing Convulsive Therapy, South. M. J. **35**:375, 1942.

and cholinergic effects of the seizure was disturbed; pronounced vagal effects, including asystole for as long as seventeen seconds, occurred.

The treatment of reactions due to vagal hyperactivity occurring in curarized patients during and after electrically induced convulsions is not satisfactory. Neostigmine, the commonly used antagonist to the effects of curare, is ineffective in this type of reaction and, indeed, through its depressing effect on cholinesterase, may prolong or exaggerate the severity of the changes which occur. Atropine effectively prevents the vagal cardiac arrhythmias [16] occurring during electric shock therapy, but routine premedication of all patients receiving curare before convulsant therapy is undesirable; the use of this drug, by inhibiting other vagal effects, results in rises in blood pressure which are potentially dangerous [15] and prevents the antagonistic action of neostigmine on curare,[17] should the use of that drug become necessary in the treatment of respiratory paralysis; in addition, atropine may potentiate some of the toxic effects of curare.[18] Epinephrine is theoretically useful, but its effectiveness has not been studied in the reaction described in this report. Since this untoward reaction is apparently largely consequent to impurities in "intocostrin," [11b] it is evident that the use of the pure alkaloid *d*-tubocurarine is to be preferred to that of "intocostrin" in patients in which convulsive seizures are induced for therapeutic purposes.

SUMMARY

A type of reaction occurring after the injection of "intocostrin" and the administration of electric shock is discussed. It is concluded that this reaction, consisting of wheezing respiration and cardiac depression, is vagal in origin.

McLean Hospital.

16. Bellet and others [4a]; footnote 15.

17. Rosenblueth, A.; Lindsley, D. B., and Morison, R. S.: A Study of Some Decurarizing Substances, Am. J. Physiol. **115**:53, 1936.

18. Perlstein, M. A., and Weinglass, A.: Fatal Effects of Prolonged Curarization, Am. J. Dis. Child. **67**:360 (May) 1944.

EXPERIMENTAL MASOCHISM

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THE PHENOMENA of masochism seem at first sight to pose a biodynamic paradox, in that self-injurious behavior patterns appear to serve the purposes neither of self preservation nor of procreation. Consequently, Freud thought it necessary to postulate a self-destructive "repetition compulsion," or "death instinct," which every organism manifests outwardly by hostility and aggression, and inwardly by "primary masochism," involuntary processes and inevitable death.[1] Many writers,[2] however, have pointed out that from a clinical standpoint what appears to be masochistic behavior may actually or symbolically represent a gratification of unconscious dependent, sexual or other needs and that therefore the concept of primary masochism may be both unnecessary and misleading. It is our purpose here to report certain laboratory observations in animals which may throw further light on this problem.

RATIONALE AND EXPERIMENTAL METHODS

In previous experiments [3] it was shown that if an animal trained to respond to a feeding signal is subjected several times to an unexpected air blast or electric shock at the moment of food taking, the animal will acquire various persistent and progressively more generalized inhibitions, phobias, compulsions, regressions and somatic dysfunctions, which

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From the Department of Nervous and Mental Diseases, Northwestern University Medical School, and the National Foundation for Psychiatric Research.

1. Freud, S.: The Economic Problem in Masochism, in Collected Papers, London, International Psychoanalytic Press, 1924; Beyond the Pleasure Principle, ibid., 1932; New Introductory Lectures on Psychoanalysis, translated by W. Sprott, New York, W. W. Norton & Company, Inc., 1933. Menninger, K. A.: Man Against Himself, New York, Harcourt, Brace and Company, Inc., 1938.

2. Dollard, J., and others: Frustration and Aggression, New Haven, Conn., Yale University Press, 1945. Masserman, J. H.: Principles of Dynamic Psychiatry, Philadelphia, W. B. Saunders Company, 1946. Money-Kyrle, R.: Superstition and Society, London, Hogarth Press, 1939. Reich, W.: Character-Analysis, translated by Theodore P. Wolfe, New York, Orgone Institute Press, 1945. Reik, T.: Masochism in Modern Man, New York, Farrar & Rhinehart, Inc., 1941.

3. Masserman, J. H.: Behavior and Neurosis, Chicago, University of Chicago Press, 1943.

constitute an induced neurosis. In these experiments the air blasts and electric shocks appeared to act as "unpleasant" or "traumatic" stimuli, in that they served to precipitate a conflict among patterns of food seeking and those of food avoidance, with a consequent motivational impassé and failure in adaptation. Nevertheless, as a further control, it was necessary to show whether or not the "negative" effects of the traumatic stimuli could be reversed if they were made to serve as indicators of an approaching reward rather than as obstacles to its attainment; if the animals would then seek the "traumatic" stimuli even when the associated rewards were discontinued, the experimentally adaptive nature of the "masochistic" behavior would be demonstrated.

Experiments based on this rationale were conducted on 5 animals with paired controls over a period of sixteen months, and their most significant results were photographed and assembled into a motion picture.[4] Three typical experiments will be described here.

EXPERIMENT 1.—Avidity for "traumatic" stimuli. Spot, a kitten 2 months old, was trained over a period of four weeks to open a box for pellets of food in response to a light-and-bell signal. When this pattern had become well established, Spot, at the moment of food taking on six separate occasions, was subjected to an unexpected air blast (12 pounds [5.4 Kg.] pressure, 1 cm. opening, at a distance of about 15 cm.) concurrent with a condenser shock (5,000 volt, 200 milliampere, 1/50 second impulses at one second intervals) administered for five seconds through the grid floor of the experimental cage. Spot's behavior during and after these experiences became progressively neurotic: In the apparatus Spot began to show severe startle reactions, panic states or cataleptic immobility, whereas in nearly all other situations he was exceedingly inhibited, hypersensitive, phobic, stereotyped and regressive in his behavior. As a control, Spot's litter mate, Nick, was similarly trained when 2 months old to respond to a bell-light feeding signal, with the modification that after two weeks of such training the air blast and shocks were gradually made part of the feeding signals. On the first day Nick showed slight startle in reaction to the first ten combined signals, but during the succeeding twenty signals all signs of hesitation disappeared and the feeding again became prompt and spontaneous. On the second day the bell-light components of the preliminary signal were omitted; nevertheless, Nick continued to feed avidly after the air shock stimuli alone, even when the latter were made as explosive and intense as those that almost invariably induced conflictful avoidance reactions in control animals. The contrast in the behavior of the litter mates at this stage of the experiment was striking: Nick waited at the source of the air blast for the feeding signals, while Spot, cringing in a far corner of the cage, would tremble, show physiologic signs of anxiety and become immobile to the point of catalepsy in response to the same stimuli. Moreover, even after a year of rest from the experimental situation, and when both cats were fully grown, the contrast was still vivid. Nick, a healthy, active, friendly cat, opened the food box readily when an air blast was blown across it, whereas Spot, an inhibited, hypersensitive, cachectic animal, showed severe exacerbations of his neurotic reactions even when merely placed in the apparatus. Further, Spot's behavior continued to be strikingly neurotic until electroshock therapy and intensive retraining partially disintegrated some of the neurotic patterns.[4]

4. Masserman, J. H., and Jacques, M. G.: The Effects of Cerebral Electroshock in Experimental Neurosis, Am. J. Psychiat. **104**:92, 1947.

EXPERIMENT 2.—Self administration of "traumatic" stimuli. Two other kittens (Tiger and Babe in the film [5]) were trained by different experimenters not only to respond to the air blast by feeding but to operate an electric switch which released the blast. Thereafter both animals would squeeze through narrow barriers and surmount other obstacles to reach the switch in order to subject themselves to the air blast. Moreover, they would continue to do so indefinitely when the food reward was given only occasionally or was withheld up to five days—and even then the pattern could be reevoked by a few pellets. As an extension of this experiment, electric shocks (Harvard inductorium; 3 volts, primary circuit; 5 cm., secondary coil extension) were administered through the floor of the cage simultaneously with the air blasts; yet 2 cats (Nick and kitten IV) could readily be trained to press a switch and subject themselves repeatedly to "traumatic" stimuli that in other circumstances would have induced strong avoidance responses.

EXPERIMENT 3.—Self-administered traumatic stimuli and neurosis. One animal (cat 3) had been subjected to a mild hunger-fear conflict as a kitten and had thereafter, like Spot, acquired a phobic hypersensitivity to all stimuli associated with air blasts. After about three months of rest, however, the animal was induced by intensive retraining to feed after a very light air blast and then to manipulate a switch that itself released the blast. The behavior of this animal, however, differed from that of the others in that the cat always manipulated the switch hesitantly and gingerly, with head averted and paw outstretched, though once the air was released the animal rushed in its direction for the food reward. Nevertheless, it was observed in this animal and in another that if the blasts were made sufficiently strong to reprecipitate the conflict between hunger and fear, inhibitions of feeding, avoidance of the switch, overdependence on the experimenter, regressive behavior (e. g., sucking coat buttons or other sessile objects) and similar neurotic patterns appeared. In effect, the experimentally induced "masochistic" behavior had a limen which varied with the experiences of the animal, and when this limen was exceeded to the point of psychobiologic trauma the resulting motivational and adaptational conflicts became manifest in neurotic behavior.

In summary, these experiments indicate that an avidity for ostensibly unpleasant or painful experiences is not necessarily an expression of "primary masochism," but may be conditioned by the previous association of such experiences with the satisfaction of biologic needs.

SUMMARY

Cats can be trained to respond to air blasts and electric shocks as feeding signals and to administer these stimuli to themselves even after the original rewards are discontinued. The experimental production or experiential evolution of such seemingly "self-punitive" patterns may be relevant to the biodynamics of masochism.

Northwestern University Medical School (11).

5. Masserman, J. H., and Jacques, M. G.: Experimental Masochism: Motion Picture Film, Psychological Cinema Register, State College, Pennsylvania.

CANINE EPILEPSY CAUSED BY FLOUR BLEACHED WITH NITROGEN TRICHLORIDE ("AGENE")

III. Electroencephalographic Analysis

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CHICAGO

A MAJOR obstacle to the experimental approach to human idiopathic epilepsy has been the absence of a nonsurgical means of producing the characteristic intermittent grand mal attacks and cerebral dysrhythmia of the human disease.

In May 1947, investigators [1] at the University of Wisconsin observed that a diet of wheat gluten produced in the electroencephalogram of dogs an abnormality indistinguishable from that associated with human epilepsy. In December 1946, Mellanby [2] demonstrated that it was the "agene" process (bleaching of the flour with nitrogen trichloride) which made the flour a convulsant (presumably in its gluten derivatives). Numerous reports [3] confirmed Mellanby's conclusion, while further

From the Army Medical Nutrition Laboratory, 1849 West Pershing Road, Chicago 9, an installation under the jurisdiction of the Surgeon General, Department of the Army (Dr. Silver, Dr. Monahan and Dr. Pollock), and the Department of Psychiatry, Illinois Neuropsychiatric Institute (Dr. Klein).

1. Newell, G. W.; Erickson, T. C.; Gilson, W. E., and Elvehjem, C. A.: Effect of Wheat Gluten Diet on the Electroencephalograms of Dogs, Proc. Soc. Exper. Biol. & Med. **65**:115-118 (May) 1947.

2. Mellanby, E.: Diet and Canine Hysteria: Experimental Production by Treated Flour, Brit. M. J. **2**:885-887 (Dec. 14) 1946.

3. (*a*) Moran, T.: Nitrogen Trichloride and Canine Hysteria, Lancet **2**:289-291 (Aug. 23) 1947. (*b*) Radomski, J.; Woodard, G., and Lehman, A.: The Toxicity to Dogs of Various Flour Improvers, read at the meeting of American Chemical Society, New York, Sept. 18, 1947. (*c*) Silver, M. L.; Zevin, S. S.; Kark, R. M., and Johnson, R. E.: Canine Epilepsy Caused by Flour Bleached with Nitrogen Trichloride (Agene): I. Experimental Method, Proc. Soc. Exper. Biol. & Med. **66**:408-409 (Nov.) 1947.

studies [4] have shown that it is a reaction product of wheat protein and nitrogen trichloride which is the convulsant agent.

The fact that a cerebral dysrhythmia can be induced in dogs by the ingestion of an adequate diet containing large amounts of bread is a matter of significance in public health. It is of interest especially to neurologists, and it emphasizes the need for electroencephalographic studies in cases of nutritional disease affecting the central nervous system.

MATERIALS AND METHODS

Except for experiments on 3 dogs and 6 monkeys, in which serial electroencephalograms were obtained by attaching scalp electrodes to the intact animal, the bulk of this report is based on 44 acute experiments on dogs.

With the animal under vinyl ether or ether anesthesia, electrodes were screwed into the skull for recording by a Grass six channel electroencephalograph. Artificial respiration was maintained via a tracheal cannula, after paralysis had been induced with 25 mg. of dihydro-β-erythroidin hydrobromide, given intravenously, and while it was maintained with the same agent in a solution containing 1 mg. per cubic centimeter in 0.156 molar solution of sodium chloride.

The animal was prepared for intravenous infusion via the femoral vein when materials were to be tested by that route.

All animals were fed a baked control ration of flour, liver, casein, salts, sucrose, corn oil and vitamins. The details of its preparation and analysis have been reported.[3c] The experimental epilepsy-producing ration was the same except that the flour component had been treated with 30 Gm. of nitrogen trichloride gas per hundred pounds (45 Kg.) of flour. This treatment, known commercially as the "agene" process (because it artificially ages and bleaches flour) is the most widely used chemical process applied to bread flour. For this experiment, bleaching was carried out at a level ten times that of commercial practice. Details of the bleaching technic performed in our laboratory are noted in a previous report.[3c]

After two weeks of control, the dogs were switched from the unbleached to the bleached diet, and clinical observations were made, followed by electroencephalographic recordings from animals who had ingested known quantities of bleached flour.

RESULTS

The control diet, containing unbleached flour, was fed to 75 dogs and 6 monkeys for periods up to three months and was found adequate to maintain good nutrition and weight during this time, without detectable electroencephalographic abnormalities.

The bleached flour diet caused varied clinical pictures, including typical changes of conduct, ataxia, weakness and epileptic convulsions.

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4. (*a*) Silver M. L.; Monahan, E. P., and Klein, J. R. Canine Epilepsy Caused by Flour Bleached with Nitrogen Trichloride (Agene): II. Role of Amino Acids, Proc. Soc. Exper. Biol. & Med. **66**:410-412 (Nov.) 1947. (*b*) Silver, M. L.; Johnson, R. E.; Kark, R. M.; Klein, J. R.; Monahan, E. P., and Zevin, S. S.: White Bread and Epilepsy in Animals, J. A. M. A. **135**:757-760 (Nov. 22) 1947.

Fig. 1.—A seizure in a dog after nine days on the experimental diet, during which time 1,600 Gm. of bleached white flour treated with 30 Gm. of nitrogen trichloride per hundred pounds (45 Kg.) had been consumed. This animal had been on a control diet, containing unbleached flour, for thirty-one days prior to institution of the experimental diet, during which time its electroencephalogram was normal. Electroencephalograms: (*a*) at start of the convulsion; (*b*) one minute later; (*c*) one minute after *b*, at the end of the convulsion and the beginning of the postictal phase.

The top record shows the electrocardiogram; the three electroencephalographic tracings in each group are as follows: (upper) left parietal lead to ground; (middle) right parietal lead to ground; (lower) left parietal to right parietal (bipolar). Ordinate, 200 microvolts; abscissa, one second.

Frequently, the first sign of abnormality was a striking change in the attitude of the animal toward its caretakers. An aggressive animal might become retiring, or a friendly one, irritable or vicious. Some animals stood quietly and stiffly for minutes staring into space, seeming pyknoleptic. In contrast to these "standing fits," some had classic "running fits," howling and dashing wildly around the cage. At these times, ataxia, especially of the hindlimbs, was pronounced.

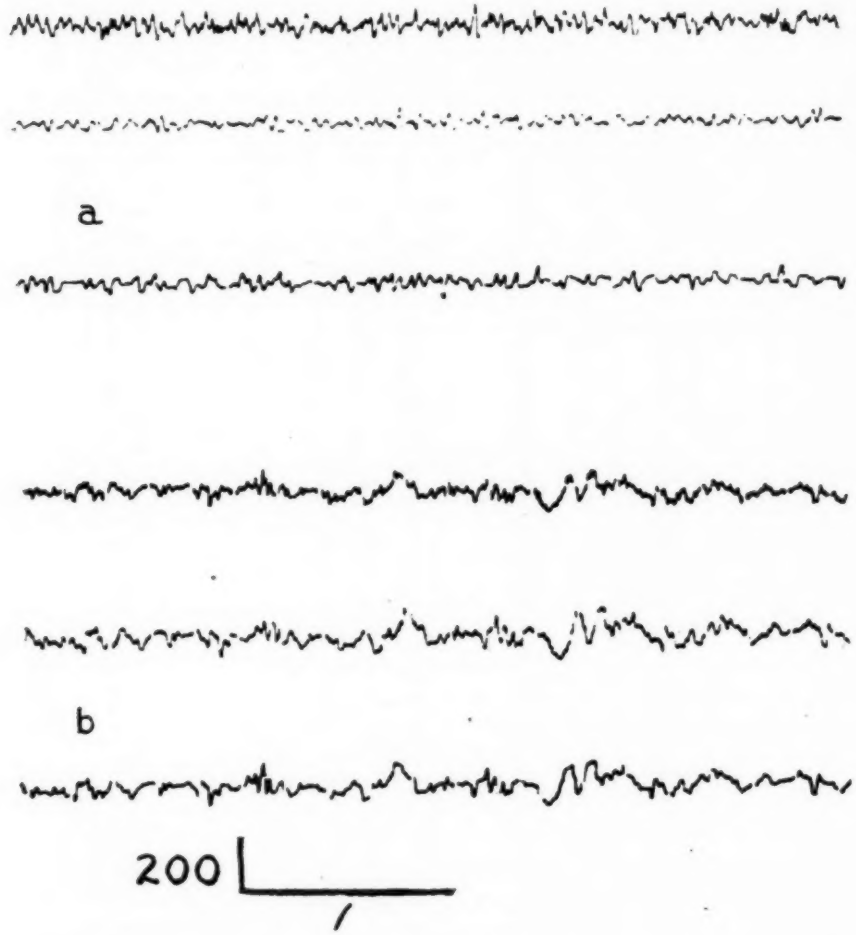

Fig. 2.—(*a*) Normal electroencephalogram of a dog maintained on a control diet for three weeks; (*b*) electroencephalogram of the dog one day after institution of experimental diet, after ingestion of 150 Gm. of white wheat flour treated with 30 Gm. of nitrogen trichloride per hundred pounds (45 Kg.).

Their grand mal attacks lasted two to five minutes, occurring either spontaneously or as a result of sudden sounds or lights (fig. 1). Each fit began with a premonitory howl, followed by falling, salivation, a short tonic period, running or paddling movements and, finally, clonic jerks, urination and defecation. In the postictal period the animal was

extremely weak, arose with difficulty, appeared bewildered and was very quiet. Usually, about thirty minutes after an attack, the dog had returned to the state before the fit. When electroencephalograms were recorded daily, a cerebral dysrhythmia resembling that of human epi-

Fig. 2 (cont.).—(*c*) Electroencephalogram of dog two days after start of experimental diet, after ingestion of 337 Gm. of white wheat flour treated with 30 Gm. of nitrogen trichloride per hundred pounds; (*d*) electroencephalogram of same dog as that whose record is shown in *c*, after intravenous injection of an agenized synthetic amino acid mixture resembling gliadin in the proportions of the individual acids, treated with 30 Gm. of nitrogen trichloride per hundred pounds.

lepsy was noted within forty-eight to seventy-two hours after the start of the agenized diet (figs. 2 and 3). If the bleached flour diet was not changed within twenty-four hours after the onset of symptoms, the

convulsive disorder continued, and some of the animals died in status epilepticus. We have noted anorexia and oliguria in some dogs within three days of institution of the experimental diet. The specific gravity of the urine dropped progressively and finally became fixed at 1.010. In

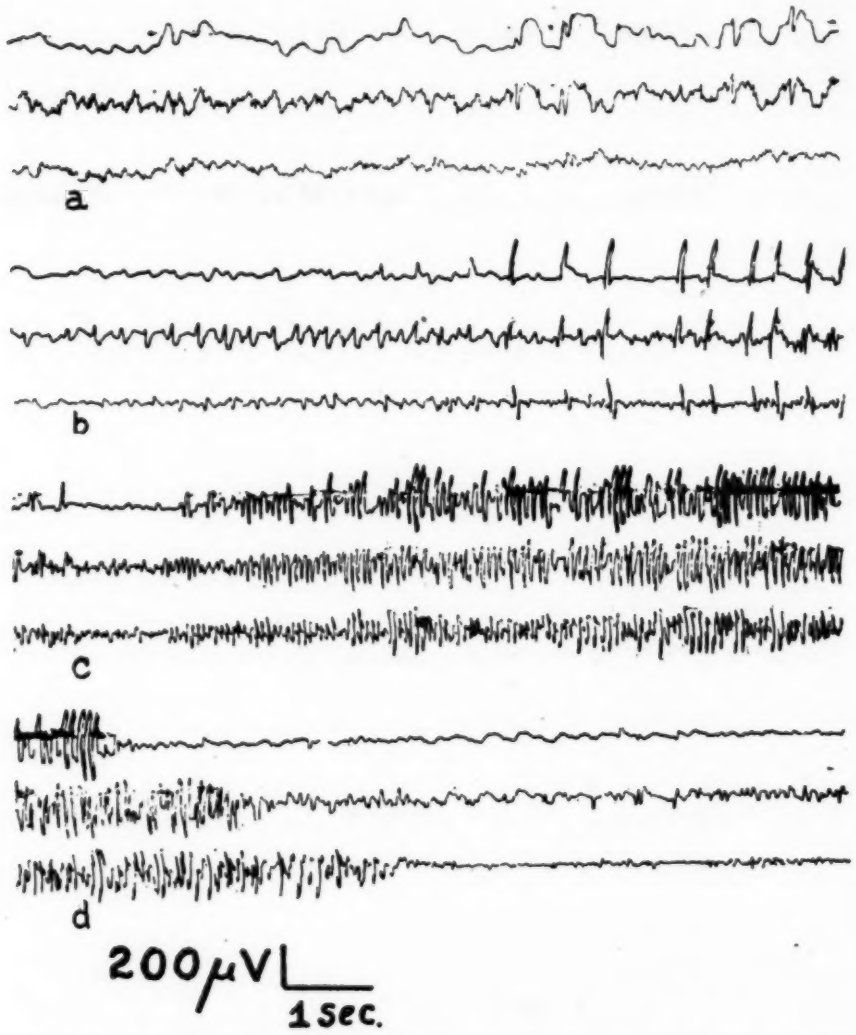

Fig. 3.—(*a*) Electroencephalogram of dog on experimental diet for three days after ingestion of 487 Gm. of white wheat flour treated with 30 Gm. of nitrogen trichloride per hundred pounds; (*b, c, d*) continuous record of seizures precipitated in the same animal by the intravenous injection of an agenized synthetic amino acid mixture resembling gliadin in proportions of individual amino acids, treated with 30 Gm. of nitrogen trichloride per hundred pounds.

the only previous description of electroencephalographic changes associated with canine epilepsy [1] the day by day changes were not noted. We feel that a careful study of the electroencephalogram, especially at

the onset of the disease, is of significance in the analysis of this type of experimental epilepsy.

The basic change in the brain waves was from the normal low voltage fast potentials to the high voltage slow activity that persists during the course of the disease. The first changes were an increase in amplitude of cortical potentials and an increased frequency, with an occasional slow wave. By the end of twenty-four hours a few high voltage slow waves had appeared (fig. 2 *b*). By the end of forty-eight hours there was a notable increase in amplitude (fig. 2 *c*) with a perceptible increase in frequency (from about twenty to thirty a second). Irregular spikes appeared, often followed by large waves of low frequency. At this stage, the abnormality in the electroencephalogram may be intensified by the intravenous administration of "bleached" amino acids [4a] (fig. 2 *d*). At the end of three days, the typical slow waves, with occasional spike and dome activity (fig. 3 *a*) appeared, and thereafter this general pattern was seen throughout the course of the disease. At this stage, the sensitivity of the animal to intravenously administered "bleached" amino acids was so great that seizures were readily induced (fig. 3 *b, c* and *d*).

The seizures induced by injection were comparable to those which occurred in animals after nine days on the experimental diet without injection. All such seizures showed a slow electrical "build up" to a full seizure discharge of the entire cortex and proceeded to the typical isoelectric postictal phase. Occasionally asymmetry of amplitude or onset in one hemisphere two to three seconds before the other was seen, but in all cases the entire brain was involved, without foci being noted.

Such seizures can be stopped by the intravenous administration of adequate amounts of "pentothal sodium" or trimethadione.

SUMMARY

The electroencephalographic abnormalities developing progressively in dogs when they ingest an otherwise nutritionally adequate diet containing 75 per cent white wheat flour bleached with "agene" (nitrogen trichloride) are shown to resemble the electroencephalographic patterns associated with human idiopathic epilepsy.

Merck & Co., Inc., donated the amino acids and the β-erythroidin. The Quartermaster Food and Container Institute, Cereal and Baked Products Branch, offered its facilities for the prosecuting of this research.

Johns Hopkins Hospital, Baltimore (5), (Dr. Silver).
1849 West Pershing Road, Chicago (Dr. Monahan).
Illinois Neuropsychiatric Institute, Chicago (Dr. Klein).
1849 West Pershing Road, Chicago (Dr. Pollock).

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

BIOCHEMISTRY OF THE SPHINGOLIPIDES: II. ISOLATION OF DIHYDROSPHINGOSINE FROM THE CEREBROSIDE FRACTIONS OF BEEF BRAIN AND SPINAL CORD. H. E. CARTER, W. P. NORRIS, F. J. GLICK, G. E. PHILLIPS and R. HARRIS, J. Biol. Chem. **170**:269, 1947.

Dihydrosphingosine has been characterized as a component of the sphingolipids of beef brain and spinal cord. It is present in a higher concentration in spinal cord than in brain. This is the first observation of the occurrence of dihydrosphingosine in nerve tissue of higher animals, although Lesuk and Anderson isolated it from Cysticercus fasciolaris. Methods have been described for preparing sphingosine, dihydrosphingosine and their N-acetyl-, N-benzoyl, triacetyl and tribenzoyl derivatives.

PAGE, Cleveland.

BIOCHEMISTRY OF THE SPHINGOLIPIDES: III. STRUCTURE OF SPHINGOSINE. H. E. CARTER, F. J. GLICK, W. P. NORRIS and G. E. PHILLIPS, J. Biol. Chem. **170**: 285, 1947.

Triacetylsphingosine undergoes partial hydrogenolysis of an acetoxy group on catalytic reduction, indicating that the structure proposed by Klenk and Diebold for sphingosine is not correct. The failure of N-acyl-sphingosines to be oxidized by periodate and the oxidation of dihydrosphingosine to palmitaldehyde, formic acid, ammonia and formaldehyde establish the structure of dihydrosphingosine as 1,3-dihydroxy-2-amino-octadecane. These results, in conjunction with the earlier experiments of Levene and of Klenk, show that sphingosine is 1,3-dihydroxy-2-amino-octadecene-4.

PAGE, Cleveland.

Psychiatry and Psychopathology

ON ACTING. OTTO FENICHEL, Psychoanalyt. Quart. **15**:144 (April) 1946.

Fenichel states that exhibitionism is the underlying basic partial instinct in acting. Exhibitionism is especially likely to give narcissistic reassurance and erogenous pleasure simultaneously.

The sexual pleasure consists in using the spectator to satisfy the exhibitionist's narcissistic needs. Actors supply their dependent needs by a sublimated and desexualized exhibitionism and thereby counteract inner fears.

The aims of acting are approached by "playing parts." As in children's play, playing is a process of learning while developing the abilities to master the outer world. At the same time it may be anticipatory, in that it creates tensions which might occur, but at a time and in a degree which is determined by the participant himself, and which therefore is under control. The actor acts by assuming emotions which he does not have, but which he might have; or he displaces tensions, which he once experienced in his past, onto imaginary persons and abreacts unmastered tensions in identification with them. In his "parts" the actor shows himself, but not as he really is. In pretending to be somebody else, he does not show himself, but, rather, conceals himself.

Besides the direct narcissistic satisfaction that the actor receives from applause, there is a narcissistic satisfaction from a sense of magical influence on the audi-

ence. This influence may be directed toward compelling the audience to applaud, toward threatening the audience, or at least toward showing the actor's own superiority and power, which is needed for soothing anxiety, probably in an apotropaic way.

The artist, especially the actor, in presenting his work, which unconsciously represents an expression of repressed instinctual wishes, induces his public to participate in his forbidden wishes through acceptance and praise of his work. If he succeeds, his feelings of guilt are removed or decreased.

The unconscious aims of the magic influence which the actor tries to convey to his audience are usually two: seduction to participate in the actor's guilt, and the craving to gratify passive oral needs by any means, including, if necessary, destruction or castration of the audience. Acting has a deep connection with the castration complex and serves the purpose of denying castration and of influencing the audience to give some equivalent reassurance. The most drastic idea of forcing the audience to give such reassurance is the unconscious fantasy of castrating the audience.

WERMUTH, Philadelphia.

UNCONSCIOUS FACTORS IN GROUP THERAPY. GERALDINE PEDERSON-KRAG, Psychoanalyt. Quart. **15**:180 (April) 1946.

Pederson-Krag studied forty groups of patients receiving group therapy. Most of the therapeutists attributed their success to education of the group members and the permissiveness of the group atmosphere. The author states, however, that in many patients the change is more than superficial, and in her studies she found evidence that unconscious emotional reactions occur. In these, as in all groups, there is ascendancy of the conscious over the unconscious in the minds of the group members. At the same time, the group is made up of individuals who have substituted the same object for their ego ideal and have consequently identified themselves with each other. All the groups studied offered the realization of preconscious fantasies which produce narcissistic gratification and a lessening of anxiety.

Pederson-Krag classified the groups in terms of the preconscious fantasies they best exemplified. The first type of group is protective. Here the group leader becomes the substitute for the good parent. Thus, the fantasy realized is "I have more powerful and more accepting parents than the people with whom I live." The second type is the permissive group. Here, the keynote is that the child who expects prohibition from a father substitute does not get it, despite aggression which might well call forth not only prohibition but retribution. This fulfils the child's fantasy, "I am stronger than my father. He cannot stop me from doing what I like." The narcissistic gratification afforded by such a fantasy may be expressed as, "It is as though I were grown up now." In the third type of group, the fantasy realized is "My sins are forgiven me." This is accompanied with exposure of guilt and of the wishes and attitudes concealed because of that guilt, combined with the acceptance by the group leader of such guilt and its causes. The fourth type is the magician's group, in which the patients are taught that by altering their conscious mental processes they can bring about concomitant physical changes. Here we have the fantasy "I can work magic; I say to my peptic ulcer 'Be gone,' and it diminishes." The last group operates by encouraging the members to speak of their ills, the leader being the fountain of knowledge and healing. The fantasy satisfied is "My father loves me because of my failings and hurts."

WERMUTH, Philadelphia.

Meninges and Blood Vessels

MENINGOCOCCIC INFECTIONS IN AN ARMY STAGING AREA: ANALYSIS OF 63 CASES WITHOUT FATALITY FROM THE STANDPOINT OF EARLY DIAGNOSIS AND TREATMENT. A. ALLEN GOLDBLOOM, EMANUEL H. NICKMAN and EDWARD E. P. SEIDMON, Ann. Int. Med. **24**:589 (April) 1946.

This study was undertaken in an attempt to gain a better understanding of two major problems in the treatment of patients with meningococcic infections. The first problem was early diagnosis prior to localization of the organism in the meninges, especially in sporadic cases, and the second was the optimum dose of sulfonamide drug.

Sixty-three consecutive patients with meningococcic infections were treated at the hospital of an Army port of embarkation during the period from July 4, 1942 to July 4, 1945. This group represents the total incidence in slightly over 1,000,000 processed, seasoned troops. The disease was sporadic.

Diagnosis is frequently difficult and delayed in interepidemic periods. The value of early signs and symptoms in establishing a diagnosis is emphasized.

Therapy is most effective during the first twenty-four hours of illness. All patients, regardless of their clinical appearance, must be considered seriously ill and treated accordingly. Intravenous therapy is the most rapid and satisfactory means of securing a therapeutic effect of the sulfonamide drug. Sodium sulfadiazine is recommended as the drug of choice for initial medication in all cases of meningococcic infection, regardless of severity. Sulfadiazine and its sodium salt were the only chemotherapeutic drugs used. The average total dose per patient was 54.7 Gm. No correlation was found between sulfadiazine concentrations in the blood and the clinical response obtained.

Complications due to the disease and toxic reactions following the use of sulfadiazine were negligible. All patients were returned to duty, and there were no fatalities.

GUTTMAN, Philadelphia.

MIDLINE CALCIFIED INTRACRANIAL ANEURYSM BETWEEN OCCIPITAL LOBES. DANIEL OSCHERWITZ and LEO M. DAVIDOFF, J. Neurosurg. **4**:539 (Nov.) 1947.

Oscherwitz and Davidoff add a fifth case of an anomalous anastomosis of the great vein of Galen with branches of the circle of Willis. A woman aged 27 was admitted to Montefiore Hospital complaining of headache of nine months' duration. The headaches were deep in the vertex; they were sharp, lasted up to two or three weeks and were followed by periods of relief of about the same duration. Three to four months previous to admission, the patient had noted intermittent blurring of vision, with no diplopia. Visual acuity appeared normal at this time. The results of neurologic and physical examinations were normal, as were those of all laboratory studies except the roentgenograms of the skull. These showed an irregular mass with calcified borders, 3.5 cm. in diameter, lying in the midline posterosuperior to the pineal gland. Hydrocephalus was not evident in the encephalogram. A ventriculogram showed some indentation on the inner aspect of both posterior horns.

At operation, a mass was observed near the free edge of the falx and the incisura of the tentorium, pushing the falx to the right. Exploration and puncture of the mass revealed a gush of blood. The bleeding was stopped and the wound closed. After operation there was a left homonymous hemianopsia, which subsided in five days. The headache improved greatly, and the patient was asymptomatic when seen one year later.

The absence of hydrocephalus was probably due to the patency of the aqueduct and the normal ventricular flow. The relief of symptoms was possibly due to thrombosis of the lesion after puncture. The question of operation is left open by the authors. In cases of obstructive hydrocephalus a short circuiting operation should be performed.

TOZER, Philadelphia.

OBSERVATIONS ON PLAGUE MENINGITIS. D. LANDSBOROUGH and N. TUNNELL, Brit. M. J. **1**:4 (Jan. 4) 1947.

In a series of 203 cases of plague at the general hospital, Chuanchow, South China, between 1943 and 1945, there were 8 cases with meningeal involvement, in 1 of which occurred the rare clinical form recognized as primary plague meningitis (clinical picture of meningitis without bubo formation). The clinical features closely resembled those of acute meningitis. Special symptoms included convulsions, disturbances of the cranial nerves, vestibulocerebellar symptoms, deep coma and vasomotor crisis. The diagnosis offered little difficulty. Treatment consisted of administration of sulfathiazole; intrathecal injection of plague serum, in most cases; daily lumbar puncture for drainage of the subarachnoid space, and cisternal puncture when lumbar puncture proved unsatisfactory.

ECHOLS, New Orleans.

TEMPORAL ARTERITIS. MICHAEL KREMER, Proc. Roy. Soc. Med. **40**:84 (Dec.) 1946.

A woman aged 75 experienced severe pain over the left side of the head and in the back of the neck, accompanied by tenderness of the left side of the scalp, poor general physical condition and a febrile course. Three months later amblyopia developed bilaterally and her left leg became weak. She showed atrophy of the optic nerves and spastic paresis of the left leg. Section of the temporal artery on the left showed recanalization of a previously thrombosed lumen, with chronic inflammatory infiltration and occasional giant cells in the wall. Although the signs remained stable, the patient's physical condition improved. Clinically, she showed involvement of the middle cerebral artery and occipital artery, as well as of the temporal and ophthalmic arteries.

BERRY, Philadelphia.

TUBERCULOUS MENINGITIS TREATED WITH STREPTOMYCIN. M. MURSA, J. B. DOS REIS and J. RENATO WOISKI, Arq. de neuro-psiquiat. **5**:135 (June) 1947.

This is the first case of recovery from tuberculous meningitis treated with streptomycin reported in Brazil. A child aged 5 years with typical tuberculous meningitis was treated with streptomycin and apparently recovered. The organisms were isolated from the spinal fluid, and their virulence was proved by animal inoculations. The treatment was started on the eighth day of illness and was continued seventy-one days. The child was given 44,650,000 units of streptomycin (42,600,000 units intramuscularly and 1,950,000 units intrathecally). At the time of writing the patient had not received treatment for forty days; the neurologic status was normal, and behavior was normal. "Promin" (sodium p-p'-diaminodiphenylsulfone-N-N'-didextrose sulfonate) was added during the last five days of treatment. The authors do not believe that the latter played any role in the child's recovery. The last lumbar puncture, while the patient was clinically well, showed 71 lymphocytes per cubic millimeter, an increase in total protein and normal sugar

and chlorides. The authors state that it was still too early to consider that the child is completely and permanently recovered.

N. Savitsky, New York.

Subarachnoid Hemorrhage Caused by Insolation: Report of a Case. D. R. Bueno and L. Urquia, Bol. Inst. de pat. med. **1**:227 (Dec.) 1946.

A fisherman aged 47, who was corpulent and moderately alcoholic, was exposed to the rays of the sun from 5 a. m. to midday. His cap did not protect him adequately from the sun. On returning to work, he complained of severe pain in the neck, which radiated anteriorly. There was some nausea. Soon after the onset, rigidity of the neck, a temperature of 37.7 C. (99.9 F.) and a blood pressure of 230 systolic and 130 diastolic were observed, and the face and hands were extremely erythematous. The following day he complained of severe pain in the back of the neck. Rigidity of the neck was still present, though less pronounced. The tendon reflexes were diminished, and the blood pressure was 140 systolic and 70 diastolic. On the third day meningeal signs were still present, and the blood pressure was 140 systolic and 70 diastolic. Lumbar puncture showed a rose tinge of the fluid, which was the same in the two tubes; the blood did not clot. Removal of 20 cc. of spinal fluid gave immediate relief. A few days later another lumbar puncture showed xanthochromic fluid. The patient's condition cleared in a few days. He was given daily intravenous injections of 4 cc. of 15 per cent magnesium sulfate. At the time of the report, a year after this acute illness, the patient was still well. The authors are sure that insolation was the cause of the subarachnoid hemorrhage.

N. Savitsky, New York.

Diseases of the Brain

The Genetics of Epilepsy. W. G. Lennox, Am. J. Psychiat. **103**:457, 1947.

Lennox studied the incidence of epilepsy among 12,119 of the near relatives of 2,130 epileptic patients and among 55 pairs of twins affected with seizures. He also analyzed the electroencephalographic records of 470 relatives and of the 55 twins.

Of the members of the immediate families of epileptic patients, 2.7 per cent had a history of recurrent seizures. This was about five times the incidence of epilepsy among draftees in World War I. But, of the 2,130 patients in this series, only 17 per cent knew of any blood relative who was similarly affected. Inheritance, as judged by the number of epileptic relatives, is only 40 per cent as great in cases of acquired (symptomatic) as in cases of genetic (essential) epilepsy. The incidence of epilepsy among relatives is greater in the group with symptomatic epilepsy than in the general population. Hence, a genetic factor is present even in the group with acquired epilepsy. Lennox concludes that epilepsy per se is not inherited, but that a tendency or predisposition is inherited.

Various factors may modify the weight of heredity. The genetic factor is greater in females than in males. Epilepsy tends to begin earlier in the life of females; the percentage of epileptic relatives is greatest if the condition begins early in the life of the patient. Patients with seizures associated with lesions of the brain have relatively few epileptic relatives, in contrast with the much larger number for patients with petit mal seizures, which rarely accompany cerebral lesions. There were more epileptic relatives if the patient was mentally defective, especially if he was mentally defective at birth.

The study of twins revealed that in 94 per cent of monozygotic twins, both co-twins were epileptic. This percentage was reduced to 17 if the epileptic co-twin

showed evidence of a pathologic condition of the brain. In only 1 of the dizygotic pairs did epilepsy occur in both co-twins.

Since the electroencephalogram is an hereditary pattern, the records of the brain waves were studied because of the possibility that irregularities in these waves may constitute the predisposition to epilepsy. In the group of 470 near relatives, some degree of abnormality was noted in 50 per cent, as against 16 per cent for the adult normal control groups. Electroencephalograms were made of both parents of 140 patients. For 24 per cent of the patients, the records of both parents were in some degree abnormal. In 25 per cent of the families, one or both parents had grossly abnormal records. In the group of identical twins, in which 1 of the co-twins had epilepsy and cortical dysrhythmia, the electroencephalographic record of the normal co-twin was almost always abnormal also.

FRANKEL, Philadelphia.

ROLE OF PINEALOMAS IN THE CAUSATION OF DIABETES INSIPIDUS. GILBERT HORRAX, Ann. Surg. **126**:725 (Nov.) 1947.

Horrax reports 5 cases of diabetes insipidus in which tumors of the pineal body were present. In 2 cases the nature of the growth was verified by histologic section, while in the 3 remaining cases both neurologic and roentgenologic evidence of tumors in the pineal region was present.

Diabetes insipidus with suprasellar or chiasmal lesions is understood to be the result of direct pressure on the hypothalamus or hypophysis by the tumor. Occasionally, however, these symptoms occur with tumors arising from the pineal body and apparently confined to this area. The existence of the supraopticohypophysial tract, operating as a functional unit in a hypothalmicohypophysial system, has been confirmed by Jones. The interruption of this tract or injury to any part of it may cause diabetes insipidus.

The author has shown histologically in 2 cases that pineal cells invade this region of the supraopticohypophysial tract. In the 3 remaining cases there was probably a similar invasion from a primary pineal tumor. Roentgen treatment in the last 3 cases relieved considerably the diabetes insipidus in 1, and probably in the other 2.

TOZER, Philadelphia.

OSTEOMYELITIS OF THE BASISPHENOID AND BASIOCCIPUT WITH MENINGITIS AND CRANIAL NERVE PALSIES AS A COMPLICATION OF NASOPHARYNGEAL PACKING FOR CONTROL OF EPISTAXIS. ARTHUR A. SPAR and HENRY L. WILLIAMS, Arch. Otolaryng. **46**:473 (Oct.) 1947.

Spar and Williams report the case of a man aged 48 who complained of headache, dysphagia and indistinct speech. These symptoms followed the continuous use of nasopharyngeal packing for the control of epistaxis. Nine weeks after onset the examination revealed loss of weight, purulent discharge from an inflamed and edematous nasopharynx and paresis of the right twelfth nerve. Nuchal rigidity with involvement bilaterally of the ninth, tenth and twelfth cranial nerves and of the motor division of the left fifth cranial nerve developed rapidly. The changes in the spinal fluid were those of serous meningitis. Roentgenograms of the skull, sinuses and base of the cranium were normal. Cultures of the discharge were sterile.

Treatment with sulfadiazine and penicillin and intranasal application of radium was followed by gradual improvement. At operation a cavity of pus was observed

to extend posteriorly on the surface of the basisphenoid and basiocciput. The patient was discharged on the fifty-fifth day with no residual sign other than incomplete function of the right hypoglossal nerve.

The authors believe that this report constitutes the first instance of recovery from such a condition, and they state that the use of radium was beneficial in disrupting the protective barrier around the diseased region, thus permitting the antibiotic agents better access to the supposed organisms producing the disorder.

FARMER, Philadelphia.

BRUDZINSKI'S SIGN IN CEREBROMENINGEAL HEMORRHAGE. C. W. OLSEN and W. R. ROSANOFF, Bull. Los Angeles Neurol. Soc. **12**:139 (Sept.) 1947.

Olsen and Rosanoff investigated Brudzinski's neck and leg signs in relation to tonic neck reflexes and to meningeal irritation in cases of cerebromeningeal hemorrhage. In some cases, when both meningeal irritation and hemiplegia were present, passive flexion of the neck caused flexion of the hip and knee on the sound side only, with no visible response in the paralyzed lower extremity; in other cases passive flexion of the hip with extension of the knee on the paralyzed side caused drawing up of the leg on the sound side, while similar manipulation of the sound limb did not elicit any visible response from the paralyzed limb. These observations suggested to the authors that meningeal irritation, aggravated by tension on the spinal roots, excites the Brudzinski response and that this sign is not a postural reflex released by removal of cerebral inhibition.

FRANKEL, Philadelphia.

CEREBRAL SYMPTOMS RESULTING FROM OVERDOSAGE OF CARBARSONE. K. O. VON HAGEN, N. E. CARL and N. W. BROCKMAN, Bull. Los Angeles Neurol. Soc. **12**:148 (Sept.) 1947.

Von Hagen and Brockman report 2 cases in which there developed convulsions, coma, mental confusion and fever after the administration of an overdose of carbarsone. One patient had taken 9.75 Gm. orally and 3.12 Gm. by suppository during a period of about two weeks, apparently under the impression that she had been given a sedative. The other patient had taken 2 Gm. a day orally for five days for the treatment of intestinal parasites. Though the urine was negative for arsenic in the second case, it was felt that the clinical picture in each case was consistent with the clinical diagnosis of arsenical encephalopathy. The authors believe that the administration of carbarsone in doses in excess of 5 Gm. in ten days may result in serious complications.

FRANKEL, Philadelphia.

HEMIPLEGIA IN YOUNG ADULTS. G. JOLY DIXON, Brit. M. J. **2**:53 (July 12) 1947.

Dixon made a study of 35 patients with unilateral palsy due to involvement of the pyramidal tract seen between 1940 and 1946, in an effort to determine the etiologic factors of such an accident in young adults. Nineteen patients had only minor degrees of hemiparesis, the onset of which was insidious. Of these 19 patients, the paralysis was associated with cerebral tumor in 7, disseminated sclerosis in 6, congenital hemiparesis in 3, hysteria in 2 and syringomyelia in 1.

The stroke was sudden in the remaining 16 patients, 2 of whom had cerebral emboli during the course of rheumatic mitral stenosis with pulmonary infarcts and bacterial endocarditis; another experienced a Herxheimer reaction during treatment for secondary syphilis; a fourth probably had a cerebral aneurysm, and a fifth

had hemiplegia whenever she received an overdose of insulin. In the remaining 11 patients the etiologic factor was not so easily determined, but it was noted that the paralysis was frequently associated with sepsis in the jugular vascular bed, recent pulmonary disease and a tendency to abnormal elevation of blood pressure.

This study suggests that strokes resulting in permanent hemiplegia are not an uncommon accident in young adult life. Most such patients show no evidence of cardiac disease likely to give rise to emboli, although a few do. Dixon believes that this phenomenon is due either to venous thrombosis in the rolandic system of veins or to hemorrhage, thrombosis or embolus in the cerebroarterial system.

ECHOLS, New Orleans.

PITUITARY BASOPHILISM. G. A. PENNINGTON, R. KAYE-SCOTT and R. J. WRIGHT-SMITH, Lancet **2**:684 (Nov. 8) 1947.

The authors report the case of a woman with pituitary basophilism who was followed closely for five years, from ten months after onset of symptoms until death. The patient, a woman aged 23, had the presenting symptoms of gain in weight, hirsutism, amenorrhea and a sensation of pressure between the zygomas. Examination revealed well marked increase of subcutaneous tissue of the face, neck and trunk. The body shape and the distribution of pubic hair were male in type; the breasts and vaginal orifice were small. There was some tenderness on the right side of the abdomen over the kidney. Otherwise, the physical and neurologic status was normal. The basal metabolic rate was — 18 per cent. The visual fields were normal. A roentgenogram showed a questionable mass overlying the upper pole of the right kidney, but its presence was not confirmed on repeated examinations. Three months after her admission high voltage roentgen therapy to the area of the pituitary was begun, without benefit. Two months later a course of high voltage roentgen therapy to both adrenal areas was given, and four months after this the menses recurred and some improvement in general health and strength was noted. The improvement lasted about one year, when the symptoms returned. High voltage roentgen therapy to the right adrenal area was given, without benefit. Similar treatment was then administered to the pituitary region, likewise without benefit. One year after the last treatment, high voltage roentgen irradiation of the left adrenal area was followed by return of the menses. During the following year similar therapy to both adrenal glands was continued, with some benefit. In the fifth year, despite treatment, her weight increased, hirsutism returned and edema of the legs and dimness of vision developed. The blood pressure was now 230 systolic and 145 diastolic. There were numerous subcutaneous ecchymoses. Roentgenograms of the pituitary and adrenal areas were still normal. The fundi showed hypertensive retinitis; the visual fields were restricted, and the patient became almost blind. After several severe attacks of asthma she died. Autopsy revealed large, firm adrenal glands, with a wide hypertrophied cortex, which showed hyperplasia microscopically. The pituitary gland was small; the anterior lobe was yellowish and soft, the posterior lobe being replaced by a small cyst containing mucoid material. Microscopically, the cyst appeared to have arisen in the hypophysial stalk and left a small rim of posterior lobe. There were well marked hyaline changes in the cytoplasm of the basophilic cells of the anterior lobe and no basophil cells in the remaining portion of the posterior lobe. The kidneys presented a picture of nephrosclerosis.

MADOW, Philadelphia.

VON RECKLINGHAUSEN'S DISEASE. A. DICKSON WRIGHT, Proc. Roy. Soc. Med. **40**:49 (Dec.) 1946.

A girl aged 7 years had at birth a large pigmented nevus over the entire right side of the chest. Nodules and café au lait spots developed after birth. A diffuse, nodular, tender tumor of the left pectoral and axillary region, of recent occurrence, was removed; examination revealed a large racemose tumor with enlargement of the mammary gland due to an overgrowth of connective tissue, such as is often seen in the vicinity of the plexiform neuromas of neurofibromatosis.

BERRY, Philadelphia.

TUBEROUS SCLEROSIS WITH INTRACRANIAL CALCIFICATION AND LESIONS OF BONE. HELEN DIMSDALE, Proc. Roy. Soc. Med. **40**:81 (Dec.) 1946.

A case is described demonstrating that tuberous sclerosis may occur in association with generalized tissue dysplasia.

BERRY, Philadelphia.

THALLIUM INTOXICATION. J. VAN LAERE, J. belge de neurol. et de psychiat. **47**:40 (Jan.) 1947.

Thallium intoxication is characterized first by gastrointestinal symptoms, consisting of nausea, vomiting and diarrhea. Then, manifestations of involvement of the nervous system are noted, all portions of the central and peripheral nervous systems being affected. The most conspicuous symptoms may be those of polyneuritis with paralysis and atrophy, choreiform movements or even epileptic attacks. Involvement of the vegetative nervous system causes diffuse alopecia, with falling of the hair of the beard and of the outer portion of the eyebrows, but with no involvement of the eyelashes or the inner part of the eyebrows. Psychic manifestations include insomnia, irritability and sometimes hypersomnia and lethargy. Van Laere reports 4 cases of thallium poisoning in one family, all of whom were children; it was found that a rat poison containing thallium sulfate had been used in the home. Thallium is also employed as a depilatory and in the manufacture of artificial precious stones.

DEJONG, Ann Arbor, Mich.

UNILATERAL PARALYSIS OF THE CRANIAL NERVES DUE TO A BASAL TUMOR WITH ASSOCIATED HOMOLATERAL HYPERTROPHY OF THE FACE AND TONGUE. MICHEL J. ANDRÉ, J. belge de neurol. et de psychiat. **47**:115 (Feb.) 1947.

André reports a case of homolateral paralysis of the fifth, seventh, ninth, tenth and eleventh nerves, and possibly the sixth nerve, on the left side associated with a tumor of the greater wing of the sphenoid bone on that side. An unusual feature was hypertrophy of the face and tongue on the same side as the palsies of the cranial nerves.

DEJONG, Ann Arbor, Mich.

CORTICAL ATROPHY OF THE CEREBELLUM. LUDO VAN BOGAERT and PIERRE BORREMANS, J. belge de neurol. et de psychiat. **47**:240 (May) 1947.

Van Bogaert and Borremans report a case of cortical atrophy of the cerebellum with gliosis not only of the white matter but also of the connections with the striatum and hypothalamus. Degenerative changes were observed in the basal ganglia. It is of interest that 2 brothers of this patient had parkinsonism. Four members of the immediate family and 7 other distant relatives had apoplexy, angina

pectoris or arterial hypertension, and 2 others had diffuse cerebral disease of unknown type with confusion and other mental symptoms.

DEJONG, Ann Arbor, Mich.

LATE CEREBELLAR ATROPHY OF THE MARIE-FOIX-ALAJOUANINE TYPE OF HEREDITARY AND FAMILIAL ORIGIN WITH PARTIAL SUBCLINICAL ATROPHY OF THE GLOBUS PALLIDUS. LUDO VAN BOGAERT, J. belge de neurol. et de psychiat. **47**:268 (May) 1947.

Van Bogaert reports the case of a family in which there were 5 members with late cerebellar atrophy of the Marie-Foix-Alajouanine type. Pathologically, there was evidence of partial atrophy of the globus pallidus. Van Bogaert expresses the belief that the atrophic process had extended from the cerebellum to the pallidum and that the final clinical picture was the result of involvement of both structures.

DEJONG, Ann Arbor, Mich.

ORGANIC CEREBRAL SYNDROME IN THE HEREDITARY ATAXIAS. H. K. KNOEPFEL and J. MACKEN, J. belge de neurol. et de psychiat. **47**:314 (May) 1947.

Knoepfel and Macken, in mental tests on 15 patients with hereditary ataxia, found definite organic cerebral syndromes with emotional lability, irritability, loss of comprehension, poverty of association and general intellectual impairment.

DEJONG, Ann Arbor, Mich.

SUBDURAL HEMATOMA. H. VALLADARES, F. R. PERINO and S. VILCHES, ACTAS Cong. sudam. de neurocir. **1**:354 (March) 1945.

The authors report 37 cases of subdural hematoma, constituting 4 per cent of 816 cases of acute and chronic head trauma. In 15 of the cases the hematoma was acute and developed within two weeks. In all the cases a membrane was formed. Acute subdural hematoma usually develops in cases of very severe trauma. The mortality in acute cases is high. The authors believe that the frequent intensification of symptoms following removal of the hematoma is the result of cerebral edema at the site of compression. In 22 cases subdural hematoma developed a few weeks to a few months after the head trauma. The clinical picture in the chronic cases is that of greatly increased intracranial pressure. There was a history of head trauma in all the cases. The authors note the frequency of fluctuating coma. In 13 cases there was a history of alcoholism. The authors believe that alcohol may play an accessory etiologic role in accounting for the bleeding (perhaps the avitaminosis of alcoholism predisposes to bleeding). The neurosurgeon is considered more qualified than the neurologist to decide on indications for trephination. In 25 of the cases monoplegia or hemiplegia was found. In 18 cases there was unilateral dilatation of the pupil. Anatomic studies led the authors to agree with the theory that this sign is probably due to compression of the third nerve as a result of herniation of the brain at the base. In 1 case there was severe mental disturbance, with confusion, memory defect and aggressiveness, which required transfer to a psychiatric hospital. The authors observed localized and generalized convulsions, but they give no statistics. Membrane formation was noted as early as the third day.

N. SAVITSKY, New York.

ACCIDENT DUE TO CISTERNAL PUNCTURE IN A CASE OF CONGENITAL HYDROCEPHALUS. AFFONSO SETTE JR., Arq. assist. psicopat. estad. São Paulo **10-11**: 243 (Jan.-Dec.) 1945-1946.

An 8 year old white boy, an idiot, had had weakness of the lower limbs since early life, with flaccid paralysis and atrophy of these extremities, absence of tendon reflexes and inability to sit up or talk. A cisternal puncture was done in order to inject air; 15 cc. of a rose-colored fluid was removed. Each cubic millimeter of spinal fluid contained 33.4 red blood cells. After the cisternal puncture the patient collapsed, with cessation of respiration and heart beat. Postmortem examination showed cerebellar herniation and compression of the medulla. Hydrocephalus was due to congenital stenosis in the region of the aqueduct of Sylvius with hyperplasia of the periependymal spongioblastic tissue.

N. SAVITSKY, New York.

CACHEXIA NERVOSA AND SIMMONDS' DISEASE. R. REPETTO, J. IANNI and I. BENZECRY, Prensa méd. argent. **34**:362 (Feb. 21) 1947.

Cachexia nervosa is the term used to designate the more serious form of anorexia nervosa. Oppenheimer, Farquharson and Hyland denied that cachexia nervosa can develop into hypophysial cachexia, or Simmonds' disease. The authors report a case illustrating the possibility of such a transition and point out that previous students of the subject did not have determinations of 17-keto steroids to help them in studying the problem.

A girl aged 17 went on a drastic reducing diet in July 1943. For a while she had only 12 lemons a day as her sole nourishment. When she began to diet, she weighed 82 Kg. In January 1944 she began to complain of severe anorexia and epigastric distress. Menstruation stopped in November 1943. During January 1944 she weighed 50 Kg. Axillary and pubic hair were still present. The blood pressure was normal; the basal metabolic rate was —12 per cent, and the blood sugar measured 82 mg. per hundred cubic centimeters. After a short period of temporary improvement, the patient weighed 47 Kg., in May 1944. During June 1945 she reentered the hospital for the third time. She had vomiting and edema of the face and upper limbs; her weight was 32 Kg., and the basal metabolic rate was —36 per cent; the blood sugar was 54 mg. per hundred cubic centimeters, with a flat sugar tolerance curve. The blood cholesterol was 180 mg. and the calcium 95 mg. per hundred cubic centimeters. There were no 17-keto steroids in a twenty-four hour specimen. During March 1946 she weighed 26 Kg., was emaciated and showed atrophy of the breasts and absence of axillary and pubic hair. She died on March 26, 1946. Autopsy was not done.

The authors conclude that anorexia nervosa may develop into Simmonds' cachexia. The development may be followed by noting the point of disappearance of 17-keto steroids from the urine. Early Simmonds' disease should be suspected during the course of anorexia nervosa when the blood sugar falls below 45 mg. per hundred cubic centimeters. The authors do not believe that the onset of amenorrhea is the point of such transformation.

N. SAVITSKY, New York.

Diseases of the Spinal Cord

RELATIONS OF NERVE ROOTS TO ABNORMALITIES OF LUMBAR AND CERVICAL PORTIONS OF THE SPINE. J. JAY KEEGAN, Arch. Surg. **55**:246 (Sept.) 1947.

In the cervical and lumbar regions of the spine lesions of a single nerve root produce a clinically demonstrable hypalgesic area of characteristic distribution.

Since a herniated intervertebral disk is the frequent cause of such a radicular lesion, it is possible to identify the involved nerve root either by spontaneous pain or by hypalgesia in its corresponding dermatome. Difficulty may arise as to the locus of root compression in relation to the structures of the spine. Cases of lumbarization or sacralization or of absence of the twelfth rib may make it difficult to determine the vertebral level if one follows the conventional nomenclature.

Keegan points out that the position of nerve roots in relation to the lumbar portion of the spine is surprisingly constant if the vertebrae are counted in their total numerical sequence, and not on the basis of an arbitrary lumbar series, as defined by a quite variable first sacral segment and the last rib. In man, the sacrum is usually made up of a fusion of the twenty-fifth to the twenty-ninth vertebral segment, whereas in lower primates it is composed only of three segments, namely, the twenty-seventh to the twenty-ninth vertebra.

In the lumbar region a herniated nucleus pulposus compresses, as a rule, the nerve root which emerges one segment below the level of the involved disk. In the cervical region the nucleus compresses the root of its own level. Secondary rearrangement of nerve fibers in the cervical and lumbar plexuses does not materially change the ultimate radicular distribution of the fibers to the skin.

Roentgenographic abnormalities of the cervical and lumbar vertebrae should be evaluated independently of the clinical signs of root compression. Neurologic symptoms permit one to localize more accurately the ruptured disk than do roentgenographic changes, such as hypertrophic arthritic proliferations or reduction in the height of the disk.

LIST, Grand Rapids, Mich.

EXTRADURAL ARACHNOIDAL CYSTS OF TRAUMATIC ORIGIN. HOMER S. SWANSON and EDGAR F. FOUCHER, J. Neurosurg. **6**:530 (Nov.) 1947.

Swanson and Foucher report 5 cases of arachnoidal cysts. In 3 cases the cyst followed laminectomy for herniated lumbar disk; in 1 it resulted from a non-penetrating injury to the spine in the lumbar region, and in 1 there was no specific history of trauma but symptoms occurred during the hay fever season after severe paroxysms of coughing. In all cases the symptoms resembled those of the lumbago-sciatic type with involvement of the spinal nerve root due to compression of the cord or the nerve root.

The complication, rare as it is, must be thought of in all cases of laminectomy in which the symptoms fail to disappear or in which they recur later. A water-tight closure of all dural tears must be made at the initial operation. The case with symptoms following severe coughing gives still another explanation for the low syndrome of pain in the lower part of the back and sciatica. This cyst, however, was probably congenital.

TOZER, Philadelphia.

VARIATIONS IN THE SYNDROME OF THE RUPTURED INTERVERTEBRAL DISC IN THE LUMBAR REGION. F. V. KRISTOFF and G. L. ODOM, Surgery **22**:83 (July) 1947.

In addition to the usual syndromes of ruptured intervertebral disk at the fourth and fifth lumbar interspaces, Kristoff and Odom describe a series of other types of rupture of the intervertebral disks and complications and progressive changes in the simple type. Variations in the syndrome may be encountered when the rupture has taken place higher than the fourth lumbar interspace. In such instances, lateral protrusion has not occurred, or the protrusion is large enough to affect more than one or two nerve roots; the protrusion has been bilateral; two or more adjacent disks have ruptured; the main bulk of the ruptured disk is no longer attached to its

interspace but has wandered into the spinal canal, or the protrusion is so massive that it completely blocks the spinal canal and thus produces a syndrome simulating a tumor of the cauda equina.

The authors believe that myelography is not indicated in all cases, but is necessary only in cases in which clinical localization of the rupture is not possible. In all apparently clear cases of lateral protrusions at the fourth or fifth lumbar interspace, exploration of both interspaces is the rule.

FRANKEL, Philadelphia.

BONE DEFORMITY ASSOCIATED WITH MULTIPLE NEUROFIBROMATOSIS. N. C. TANNER, Proc. Roy. Soc. Med. **40**:47 (Dec.) 1946.

A woman aged 36 had first noted a lump on her right leg at the age of 4 years. She had two children, both of whom had neurofibromatosis, but the antecedent family history was negative for evidence of the disease. Physical examination revealed multiple café au lait spots and numerous sessile, pedunculated nodules on the skin, scoliosis of the spine and a large mobile subcutaneous tumor on the anterior surface of the right leg between the patella and the ankle. The right tibia was longer than the left and showed anterior bowing with thickening of the cortex. Medial bowing and cortical sclerosis of the right fibula were also present.

At operation a bilobular tumor, encapsulated except for periosteal attachments to the tibia and fibula and weighing 32.5 ounces (921 Gm.), was removed. The mass was that of a neurofibroma in the subcutaneous tissue with considerable hyperplasia of the nerve fibers and myxomatous change in several areas of the fibromatous part.

BERRY, Philadelphia.

Treatment, Neurosurgery

TREATMENT OF LOCAL EPILEPSY BY CORTICAL EXCISION. WILDER PENFIELD and HARRY STEELMAN, Ann. Surg. **126**:740 (Nov.) 1947.

Cortical localization of epileptogenic areas is now possible in many cases of focal epilepsy. The excision of such areas has proved effective in the treatment of 56 per cent of the 59 patients operated on by Penfield and Steelman. In 16 additional cases, craniotomies were performed without excision, and in none of these cases were the convulsions cured.

The commonest causes of the original lesions were: (1) head injury, (2) birth injury and (3) local infection. Excision of lesions due to birth injury gave the best results (76 per cent), with success in 50 per cent of cases of infectious foci and in 51 per cent of cases of lesions due to head injury.

The sooner the attacks occur after operation the poorer the prognosis, provided the character of the attacks is the same as before operation. A second excision should be done as soon as possible in such cases. Involvement of gyri situated near the original excised area, indicated by a different convulsive pattern, may be due to anoxia or edema and may carry a better outlook for future success.

The electroencephalogram together with the pattern of the seizure is the best means of preoperative localization. On exposure of the brain, direct cortical stimulation is used and excision of the involved area made.

TOZER, Philadelphia.

HERNIATED INTERVERTEBRAL DISK: ANALYSIS OF 90 CASES. WILLIAM T. PEYTON and DONALD R. SIMMONS, Arch. Surg. **55**:271 (Sept.) 1947.

Peyton and Simmons analyzed 90 cases of herniated disk in which operation was performed, with special emphasis on the surgical end results. The disk was considered pathologic only in cases in which a loose piece of cartilage was found lying

free in the spinal canal or in which there were definite bulging and spontaneous protrusion of the nucleus when the annulus was incised. In all other cases the findings were recorded as negative.

Eighty pathologic and 10 normal disks were found in the series. In about one-half the cases only the ruptured disk was removed; in the other half interlaminar fusion (of Gibson type) was performed, in addition to removal of the disk. The results for the two series were approximately the same. In the series of 80 cases with pathologic disk the results were satisfactory. Of 72 cases in which follow-up observations were made, there were continued pain and disability in only 3. In the 10 cases of normal disks the results were not good.

The authors conclude that simple removal of a ruptured disk is satisfactory and that improvement in results is likely to be realized by better selection of cases for operation, rather than by new operative procedures.

LIST, Grand Rapids, Mich.

SURGICAL RELIEF OF PAIN IN PARAPLEGIC PATIENTS. L. WILLARD FREEMAN and ROBERT F. HEIMBURGER, Arch. Surg. **55**:433 (Oct.) 1947.

Of 600 paraplegic patients, pain in the trunk and lower extremities was severe enough in 58 to require neurosurgical relief. Intractable pain was encountered relatively frequently with lesions of the cauda equina. Only anterolateral chordotomy, performed on 45 patients, afforded real relief, whereas decompressive laminectomy, rhizotomy and sympathectomy proved to be ineffective. The pain was completely abolished by chordotomy in 34 cases, improved in 9 cases and not improved in 2 cases.

The pain of paraplegia is presumably central and originates in the abnormal portion of the spinal cord or nerve roots. As judged from the clinical characteristics of the pain, there is a somatic and a visceral component. Somatic pain may be abolished by chordotomy below the second dorsal segment, but for complete relief of the visceral pain section of the anterolateral tract above this level is necessary. The operation should always be done bilaterally, since unilateral chordotomy may unmask pain in the previously unaffected limb.

LIST, Grand Rapids, Mich.

CARE AND REHABILITATION OF PATIENTS WITH INJURIES OF THE SPINAL CORD AND CAUDA EQUINA. W. G. KUHN JR., J. Neurosurg. **4**:40 (Jan.) 1947.

Kuhn reports the progress in 113 cases of traumatic lesions of the spinal cord. He does not consider that the majority of these patients are "hopeless, helpless and incapable of earning a living"; rather, he believes that "they can earn a living and become virtually independent," the result being due largely to their care and rehabilitation. He discusses the care of these patients on the basis of two phases: the bedridden and the ambulatory.

Bedridden Phase.—Bladder Care: The avoidance of urinary retention was the prime objective. Continuous catheter drainage with the use of tidal drainage was recommended. In many cases the patient himself was instructed in the manipulation of the apparatus. Ambulation with the catheter in place was instituted as early as possible. In all patients in whom normal bladder control and sensation did not return, automaticity and the attainment of a "social bladder" were the goals. Tidal drainage was indispensable in reaching this objective. Infections of the urinary tract were treated with penicillin, streptomycin and the sulfonamide compounds, the last being used as sparingly as possible.

Bowel Care: The use of enemas every third day was necessary until "reflex bowel" movements occurred. Mild laxatives and liquid petrolatum U. S. P. were

helpful. A regular hour for going to stool was established; this aided in the establishment of a conditioned gastric-colic reflex, with resulting automaticity.

Care of Decubitus Ulcer: Decubitus was the commonest complication noted. Its care and prevention lay in good nursing. The patient must be turned every two hours; the skin must be kept dry and clean; sheets must be free from wrinkles; the patient must be lifted, not dragged, from one position to another; hot water bottles must not be used over desensitized skin; binders are used in place of adhesive tape. Rubber rings and sponge rubber cushions are essential when the patient is in a wheel chair. If bed sores develop, two courses are open: operative and nonoperative. Penicillin jelly and sugar were used directly in the ulcer, either for spontaneous closure or for preparation of the ulcer for actual surgical closure with flaps or grafts.

Maintenance of Nutrition: A total caloric intake of from 35 to 45 calories per kilogram of ideal weight, containing from 1.75 to 4.0 Gm. of protein and 350 to 400 Gm. of carbohydrate per kilogram of weight, with supplemental multivitamin therapy, was considered adequate. The total protein, if not taken at mealtime, was supplemented with feedings of eggs and milk between meals.

Management of Pain: Chordotomy was performed on patients with complete lesions of the cord who had intractable pain. Patients with incomplete lesions were treated with narcotics, intravenous infusions of alcohol and dextrose, paravertebral block and administration of nicotinic acid; and only as a last resort was chordotomy or posterior rhizotomy performed.

Control of Spasm: Curare was found beneficial only when the dose was high enough to give an actual physical depression. Neostigmine gave only partial relief from spastic contractures. Bracing and ambulation, long a controversial problem, were found to be of little benefit to this group of patients. Surgically, either an anterior rhizotomy or section of the dorsal columns was performed.

Physical Therapy and Reconditioning: This should start from the day of the injury and continue until the patient can perform his exercises himself. Heat, massage and muscle reeducation are indispensable in the care of these patients.

Ambulatory Phase.—In nearly all cases of injury to the cord, resulting in paraplegia, the defect lies not in the skeletal system alone but, rather, in the neuromuscular mechanism. It was with this in mind that bracing and special devices were devised. The braces were designed not to bear weight but to splint the joints so that forces through these joints were transmitted in a normal manner. Ambulation was taught the patient, the type of gait depending on the level of the lesion and the psychologic desire to walk as naturally as possible. Walking was started on a ramp and was then transferred to crutches, where the patient learned proper balance, stair climbing and other everyday activities. The final step in the rehabilitation was to obtain a position or vocation for the patient. He was then ambulatory, with a goal ahead and independence within his grasp.

TOZER, Philadelphia.

HEMATOPORPHYRIN IN TREATMENT OF ANXIETY AND DEPRESSIVE SYNDROME. JEAN VINCHON, J. belge de neurol. et de psychiat. **47**:111 (Feb.) 1947.

Hematoporphyrin is of value in the treatment of anxiety and depressive states and certain forms of cyclic psychosis. It stimulates the vagus system, and is contraindicated if there is evidence of parasympathetic overactivity, particularly in states of anxiety neurosis with tachycardia, tremor and motor agitation. It is also contraindicated in obsessive states. It may be employed to augment the results of electroshock therapy but should not be used with insulin shock, as in the latter there is stimulation of the vagus system.

DEJONG, Ann Arbor, Mich.

Encephalography, Ventriculography, Roentgenography

THE PNEUMOENCEPHALOGRAM OF CEREBELLAR ATROPHY. J. P. MURPHY and ARANA ROMAN, Am. J. Roentgenol. **57**:545, 1947.

Structural abnormalities of the cerebellum may or may not be associated with cerebellar symptoms; but if the abnormalities are of sufficient magnitude they may be visualized by pneumoencephalography.

The authors describe 15 cases of cerebellar atrophy or degeneration with pneumoencephalographic evidence. In 4 cases there was either primary degeneration or secondary olivopontocerebellar atrophy. In 4 other cases the cerebellar atrophy was secondary to or associated with cerebral atrophy. The cerebellar degeneration was associated with Friedreich's disease in 3 cases. In 4 cases there was cerebellar hypoplasia with cerebral agenesis. In the latter group clinical cerebellar symptoms were not elicited.

In the pneumoencephalogram cerebellar atrophy may appear as enlargement of the cisterna magna and fourth ventricle, as widening and deepening of the interfolial sulci and fissures or as a combination of these abnormalities. Scalloping and deep fissuring of the surfaces of the hemispheres and modulation of the vermis are especially evident in cerebellar degeneration of the parenchymatous cortical type and in Friedreich's disease.

Subtentorial air above the cerebellum cannot be interpreted as evidence of cerebellar atrophy.

TEPLICK, Philadelphia.

HEMANGIOMA OF VERTEBRA ASSOCIATED WITH SPINAL CORD COMPRESSION. D. B. FOSTER and G. W. HEUBLEIN, Am. J. Roentgenol. **57**:556 (May) 1947.

A physician, aged 58, white, had noted ataxia and then weakness of both lower extremities. There were also pain between the scapulas, some difficulty in initiating micturition and numbness to the umbilicus. The symptoms progressed for a few months, and at the time of hospitalization the patient could not walk unassisted.

Examination revealed neurologic signs of a lesion at about the fourth thoracic segment of the cord. Spinal puncture with the Queckenstedt maneuver showed complete block. The spinal fluid protein was increased to 116 mg. per hundred cubic centimeters. There were some small hemangiomas of the skin.

Roentgenologic examination of the spine showed alternating linear striations in the body of the fourth thoracic vertebra, with loss of the normal homogeneous structure. The mottling extended into the laminas and proximal portions of the ribs bilaterally. "Pantopaque" (ethyl iodophenylundecylate) myelography revealed a complete block at the level of the lower margin of the body of the fourth thoracic vertebra.

With a fairly well established diagnosis of hemangioma of the vertebra and compression of the cord, roentgen therapy was started. Within six months three series were given, with an estimated tumor dose of 3,350 to 3,500 r. Improvement set in soon after initiation of therapy and continued steadily, until almost complete recovery was attained. Further improvement was noted when the patient was last seen.

The authors feel that in cases of hemangioma of the vertebra with slowly advancing myelopathy, the initial treatment of choice is roentgen therapy. An acute transverse myelitis occurring in the course of compression myelopathy is best treated by immediate decompressive laminectomy.

TEPLICK, Philadelphia.

Book Reviews

Successful Marriage. Edited by Morris Fishbein, M.D., and E. W. Burgess, PH.D. Price, $6. Pp. 547. New York: Doubleday & Company, Inc., 1947.

This book consists of articles by thirty-eight contributors (including nine women), and covers a wide variety of subjects. It is divided into five parts, starting with "Preparation for Marriage" (part I) and "The Marriage" (part II) and continuing with discussions on "Conception, Pregnancy, and Childbirth" (part III) and "The Child in the Family" (part IV). The concluding section, "Social Problems of Sex and Marriage" (part V), deals with such diverse topics as divorce, prostitution and how women adjust to marriage.

Despite the claims of the editors that the book is concerned chiefly with the subject of marriage counseling, most of the articles consist largely of restatements of facts and theories concerning the psychology and physiology of human reproduction. However, it is to be expected that in a compendium as complex as this there will be individual disagreements between authors and that topics in fields widely separated from marriage counseling will be considered. On the whole, this book is well written, informative and accurate. There are reprints of Dr. Dickinson's well known diagrams on contraception, sexual anatomy and physiology. Short bibliographies and notes are appended to many of the chapters for readers who wish to study further a given subject. The list of contributors includes distinguished men and women in the fields of medicine, sociology, psychology, anthropology, education and marriage counseling.

This book is recommended as a comprehensive reference work on the broad subject of marriage and its related fields and ought to have a wide circulation.

Four Hundred Years of a Doctor's Life. By George Rosen, M.D., and Beate Caspari-Rosen, M.D. Price, $5. Pp. 429. New York: Henry Schuman, Inc., Publishers, 1948.

The authors are both doctors of medicine and professional writers, with an obvious broad knowledge of doctors, history and language. The book is written not for the scientist but, rather, for the doctor who has had time to develop his own philosophy. The style combines the perspective of four hundred years with intimate close-ups in the form of extracts from the writings of the doctor subjects themselves.

The book is divided into ten parts, as follows: (1) Early Years; (2) School Days; (3) The Medical Student; (4) Practice of Medicine; (5) Scientist, Scholar, Teacher; (6) The Doctor Marries; (7) Doctor as Patient; (8) Doctor Goes to War; (9) Writing and Politics; (10) Reflections on Life and Death. There is a bibliography but no index.

This work makes delightful fireside reading. It gives the reader a feeling of intimacy with the characters and a perspective of medicine, with much to think about and to reread.

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